Definitions, Determinations, and Applications of LOD/LOQ/LCS Based on DoD QSM V4.1

Presenter

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US Army Corps of Engineers
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Topics

- *Introduction – Overview*
- *Limit of Detection (LOD)*
- *Limit of Quantitation (LOQ)*
- *Laboratory Control Sample (LCS)*
- *Project Applications*
- *Summary*
- *Q&A*

Detection Limits

Critical Level

MD

LT-MDL

SDL

RDL

IDE

WDE

CRV

MDV

DL

L_C

L_D

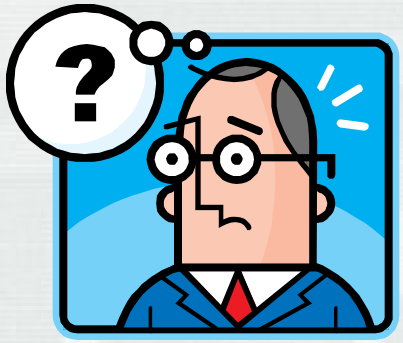
DL

CRDL

ID

LLD

LOD



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Introduction

- *For many chemical analyses, it is important to reliably determine the presence or absence of an analyte in the environment.*
- *It is equally important to quantify an analyte detected above threshold levels with a high degree of certainty.*
- *Unfortunately, the terminology we currently use to identify and discuss these threshold levels is often poorly understood and consequently misused.*

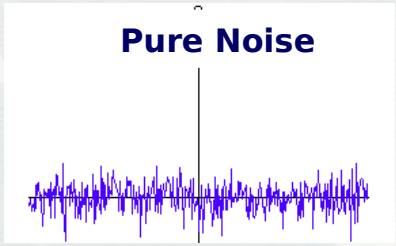
Overview of Detection/Quantitation Limits

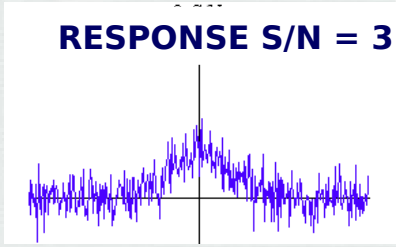
- *Analytical methods require measurement of an analytical response signal, which carries information about the analyte.*
- *A laboratory instrument must be able to detect, process, and record the analytical response signal.*
- *Response signal has two basic components:*
  - *SIGNAL: The component that carries information about the analyte.*
  - *NOISE: All other instrument responses that carry additional information not related to the analyte.*

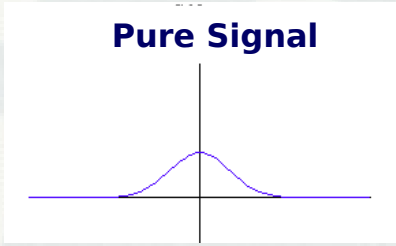
  RESPONSE = SIGNAL + NOISE

Overview of Detection/Quantitation Limit

- *Limitations of instrument responses*
  - ► *There is an instrument response level below which SIGNAL and NOISE cannot be confidently distinguished.*
  - ► *Commonly agreed at approximately S/N = 3, a RESPONSE can be confidently associated with an analyte source.*
  - ► *At or above S/N = 10, a RESPONSE can be reliably quantified.*







Method Detection Limit (MDL)

- *In 1981, staff (Glaser et al.) at EPA EMSL-Cincinnati published a procedure for determining MDL, which was later promulgated for CWA programs at 40 CFR Part 136, Appendix B in 1984.*

APPENDIX B TO PART 136—DEFINITION AND PROCEDURE FOR THE DETERMINATION OF THE METHOD DETECTION LIMIT—REVISION 1.11

The method detection limit (MDL) is defined as the minimum concentration of a substance that can be measured and reported with 99% confidence that the analyte concentration is greater than zero and is determined from analysis of a sample in a given matrix containing the analyte.

- *MDL: Minimum level that can be measured and reported with 99% confidence that it is greater than zero.*
- *Statistically-derived expression of theoretical sensitivity of analytical procedure.*
  - *7 or more spiked replicates (not burdensome for laboratories)*
  - *Multiple of standard deviation of replicates (measurement of noise)*

MDL Concept and Procedure

- *Glaser et al. assumed variability is a linear function of concentration: $s_x = b_0 + b_1 x$, where s_x is standard deviation of n replicate analyses at concentration x.*
- *MDL is defined as the concentration x, where* $t = \frac{x}{s_x / \sqrt{n}}$ *and t is the 99th percentile of Student's t-distribution with n –1 degrees of freedom.*
- *Glaser et al. made two simplifying assumptions:*
  - *Set $b_1 = 0$,* $MDL = \frac{t_{(0.01, n-1)} b_0}{\sqrt{n}}$
  - *Assume $s_x = b_0 / \sqrt{n}$* $MDL = t_{(0.01, n-1)} s_x$
- *Problems:*
  1. *Conceptual definition = L_D but mathematical definition = L_C.*
  2. *Change to a single concentration model to estimate s_x.*
  3. *Inconsistencies about whether $s_x = b_o$ or $b_0 / \sqrt{n}$, if $b_1 = 0$.*
- *Lead to underestimated MDL if spiking at a concentration < MDL.*

Source: Gibbons and Coleman, "Statistical Methods for Detection and Quantitation of Environmental Contamination" (2001)

Common Uses of the MDL

- *Method development and promulgation.*
- *Verification of laboratory performance.*
- *Monitoring trends in laboratory performance.*
- *Characterizing method sensitivity in a particular matrix.*
- *Establishing an MDL for a new or revised method for nationwide use.*
- *Used within EPA by OW, OSW, OERR, etc. and outside EPA by Standard Methods, AOAC, ASTM methods, etc.*

DoD Uses of Detection Limit

- *Comply with regulatory requirements.*
- *Assess laboratory performance.*
- *Select contract laboratories.*
- *Assess data quality.*
- *Assess data usability.*

40 CFR 136 APP B

(1) Estimate MDL based on:

- *[C] where instrument S/N = 2.5 – 5,*
- *[C] ~ 3×s of replicate instrument measures,*
- *Region of standard curve with significant change in sensitivity, or*
- *Instrumental limitations.*

(2) Prepare a minimum of 7 replicates in:

- *Reagent water: Spiked between 1 – 5× estimated MDL*
- *Other matrix: Analyze the matrix,*
  - ► *If [C] ~ 1 – 5× estimated MDL, determine MDL.*
  - ► *If [C] < 1 – 5× estimated MDL, spike and determine MDL.*
  - ► *If [C] ~ 5 – 10× estimated MDL, obtain another or accept high biased MDL.*

40 CFR 136 APP B

(3) Determine MDL:

- *Process each replicate through all sample processing steps of the entire analytical method.*
- *Make all computations according to the defined analytical methods.*
- *Calculate the standard deviation, s.*
- *MDL = t × s*

  where t is Student's t value for a 99% confidence level with n-1 degrees of freedom.

Criticisms of MDL

1. *An ideal calculation that does not represent routine operations.*
2. *Not reproducible from day to day, lab to lab, etc.*
3. *Fails to account for errors (bias) due to problems with blank water.*
4. *Does not handle non-zero blanks satisfactorily.*
5. *Does not account for variability/bias due to contaminated method blanks.*
6. *Matrix effects not always factored into MDL calculation or report.*
7. *Ambiguous relationship between MDL and IUPAC's critical level and minimum detectable concentration.*
8. *Does not assure that qualitative identification criteria can be met.*
9. *Assumes instrument response increases linearly with concentration.*
10. *Assumes constant standard deviation with concentration.*
11. *Does not require a demonstration of the ability to detect an analyte at the calculated MDL.*

Source: FACDQ (9/05)

Problems with MDL Procedure

- *Some inconsistencies between the definition and the procedure.*
- *Does not account explicitly for false negatives.*
- *Does not always yield a 1% false positive rate.*
- *Does not sufficiently account for blank bias.*
- *Does not provide a prediction or tolerance limit adjustment.*
- *Does not account for interlaboratory and temporal intralaboratory variability.*
- *Allows discretion in the use of the optional iterative procedures.*

40 CFR 136 APP B

APPENDIX B TO PART 136—DEFINITION AND PROCEDURE FOR THE DETERMINATION OF THE METHOD DETECTION LIMIT—REVISION 1.11

Definition

The method detection limit (MDL) is defined as the minimum concentration of a substance that can be measured and reported with 99% confidence that the analyte concentration is greater than zero and is determined from analysis of a sample in a given matrix containing the analyte.

Scope and Application

This procedure is designed for applicability to a wide variety of sample types ranging from reagent (blank) water containing analyte to wastewater containing analyte. The MDL for an analytical procedure may vary as a function of sample type. The procedure requires a complete, specific, and well defined analytical method. It is essential that all sample processing steps of the analytical method be included in the determination of the method detection limit.

The MDL obtained by this procedure is used to judge the significance of a single measurement of a future sample.

The MDL procedure was designed for applicability to a broad variety of physical and chemical methods. To accomplish this, the procedure was made device- or instrument-independent.

Procedure

1. Make an estimate of the detection limit using one of the following:

(a) The concentration value that corresponds to an instrument signal/noise in the range of 2.5 to 5.

(b) The concentration equivalent of three times the standard deviation of replicate instrumental measurements of the analyte in reagent water.

(c) That region of the standard curve where there is a significant change in sensitivity, *i.e.*, a break in the slope of the standard curve.

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3. (a) If the MDL is to be determined in reagent (blank) water, prepare a laboratory standard (analyte in reagent water) at a concentration which is at least equal to or in the same concentration range as the estimated method detection limit. (Recommend between 1 and 5 times the estimated method detection limit.) Proceed to Step 4.

(b) If the MDL is to be determined in another sample matrix, analyze the sample. If the measured level of the analyte is in the recommended range of one to five times the estimated detection limit, proceed to Step 4.

If the measured level of analyte is less than the estimated detection limit, add a known amount of analyte to bring the level of analyte between one and five times the estimated detection limit.

If the measured level of analyte is greater than five times the estimated detection limit, there are two options.

(1) Obtain another sample with a lower level of analyte in the same matrix if possible.

(2) The sample may be used as is for determining the method detection limit if the analyte level does not exceed 10 times the MDL of the analyte in reagent water. The variance of the analytical method changes as the analyte concentration increases from the MDL, hence the MDL determined under these circumstances may not truly reflect method variance at lower analyte concentrations.

4. (a) Take a minimum of seven aliquots of the sample to be used to calculate the method detection limit and process each through the entire analytical method. Make all computations according to the defined method with final results in the method reporting units. If a blank measurement is required to calculate the measured level of analyte, obtain a separate blank measurement for each sample aliquot analyzed. The average blank measurement is subtracted from the respective sample measurements.

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6. (a) Compute the MDL as follows:

$$MDL = T_{(n-1,1-\alpha=0.99)} \quad (S)$$

where:

MDL = the method detection limit

$t_{(n-1,1-\alpha=.99)}$ = the students' t value appropriate for a 99% confidence level and a standard deviation estimate with n-1 degrees of freedom. See Table.

S = standard deviation of the replicate analyses.

(b) The 95% confidence interval estimates for the MDL derived in 6a are computed according to the following equations derived from percentiles of the chi square over degrees of freedom distribution (χ^2/df).

LCL = 0.64 MDL

UCL = 2.20 MDL

where: LCL and UCL are the lower and upper 95% confidence limits respectively based on seven aliquots.

4. If the most recent calculated MDL does not permit qualitative identification when samples are spiked at that level, report the MDL as a concentration between the current and previous MDL which permits qualitative identification.

Reporting

The analytical method used must be specifically identified by number or title ald the MDL for each analyte expressed in the appropriate method reporting units. If the analytical method permits options which affect the method detection limit, these conditions must be specified with the MDL value. The sample matrix used to determine the MDL must also be identified with MDL value. Report the mean analyte level with the MDL and indicate if the MDL procedure was iterated. If a laboratory standard or a sample that contained a known amount analyte was used for this determination, also report the mean recovery.

40 CFR 136 APP B

- *<u>Uncertainty</u>:*
  95% confidence interval estimate for MDL based on χ^2 distribution:
  - *LCL = 0.64 MDL and UCL = 2.20 MDL*
- *<u>Optional Iterative Procedure</u>:*
  Repeat MDL study at the calculated MDL to verify the MDL and to check variances by F-test.
  - *If F-ratio < 3.05, $s_{pooled} = [(6 \times s_A^2 + 6 \times s_B^2)/12]^{1/2}$,*
    $MDL = 2.681 \times s_{pooled}$
    LCL = 0.72 MDL and UCL = 1.65 MDL
  - *If F-ratio > 3.05, re-spike at last MDL and repeat MDL study.*
- *<u>Reporting</u>:*
  - *Method, Sample Matrix, Mean Analyte Level and Recovery.*

EPA Efforts on MDL

- *On 6/8/99, EPA promulgated Method 1631B for mercury analysis by CVAFS for CWA. Shortly afterwards, Alliance of Automobile Manufacturers, et al. filed a lawsuit challenging the general procedures to establish MDL and minimum level of quantitation (ML) in Method 1631B.*
- *On 10/19/00, EPA entered a settlement agreement to perform an assessment of DL/QL.*
- *On 3/12/03, EPA issued a draft report assessing various DL/QL procedures and a proposed rule amending MDL and ML. EPA received 126 comments and withdrew the proposed rule.*
- *EPA contracted a third party to conduct a situation assessment on technical and policy issues on DL/QL and to explore the feasibility and design a stockholder process.*

Source: EPA-821-B-04-005, "Revised Assessment of Detection and Quantitation Approaches" (2004)

EPA Efforts on MDL

- *In 6/05, EPA formed a 2-year Federal Advisory Committee on Detection and Quantitation Approaches and Uses in the Clean Water Act Programs (FACDQ).*
  - *Initially 21 members from states, laboratories, industry, public utilities, environmental groups, and EPA.*
- *On 5/30/07, FACDQ renewed for 6 more months.*
- *FACDQ met 12 times from 6/21/05 to 12/21/07.*
  - *Worked on definition and use, evaluation procedure and criteria, pilot study design and evaluation, etc.*
  - *Evaluated 15 procedures, retained 9 procedures and dropped 6 procedures for further consideration.*

DL/QL Considered by FACDQ

Procedures	*DL*	*QL*	*PilotTest*
American Council of Independent Laboratories (ACIL) Procedures	*x*	*x*	*x*
Consensus Group Committee I on Detection for Proposal to EPA	*x*	*x*	
Determine DL with Lab QC, East Bay Municipal Utilities District	*x*		
Hubaux-Vos Detection Limit Procedure	*x*		*x*
ASTM Interlaboratory Detection Estimate (IDE)	*x*		*x*
EPA MDL, 40 CFR Part 136, Appendix B	*x*		
ASTM Interlaboratory Quantitation Estimate (IQE)		*x*	*x*
EPA Lowest Concentration-Minimum Reporting Level (LCMRL)		*x*	*x*
EPA Minimum Level (ML)		*x*	

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DL/QL Not Considered by FACDQ

Procedures	*DL*	*QL*	*Pilot Test*
Water Research Centre Determination and Quantitation	*x*		
ISO/IUPAC	*x*	*x*	
IIAG Sensitivity Test & Full – Range Validation Study	*x*		
Office of Solid Waste (OSW) QL		*x*	
NELAC Uncertainty Calculations			
USGS LT-MDL			

Source: FACDQ Final Report 12/28/07

Pilot Test Results

- *104 analytes by Methods 200.7, 300.0, 625, 608, and 335.4 and 55 analytes evaluated for DL/QL procedures with MQOs of RSD = 20%, mean recovery = 50 – 150%, and FP = FN ≤ 1%.*
- *ACIL procedures performed as well as or better than other procedures and met most objectives.*
- *FACDQ modified ACIL procedures and issued, "DQ FAC Single Laboratory Procedure v2.4", which uses tolerance and confidence intervals to determine DL/QL with required verifications.*

FACDQ Report

- *On 12/21/07, FACDQ published final report, "Report of the Federal Advisory Committee on Detection and Quantitation Approaches and Uses in Clean Water Act Programs".*
- *FACDQ proposed new definition and calculation procedures for detection limit, using IUPAC's L_C and L_D as conceptual definitions for detection.*
- *"DQ FAC Single Laboratory Procedure v2.4" seems to be complicate for implementation.*
- *Most technical recommendations discussed in FACDQ Report lacked technical details and were not approved by consensus.*
- *EPA continually works on DL/QL.*

FACDQ DL Procedure v2.4

- *If ≥ 50% MBs give numerical results,*

$$DL = \bar{X} + k \times s$$

where $\bar{X}$ is the mean MBs; s is standard deviation; and k is a multiplier for a tolerance limit of 99% population at 99% confidence level with n-1 degrees of freedom.

- *If < 50% MBs gives numerical results,*

$$DL = t \times s$$

where t is Student's t and s is standard deviation of measured QL spikes.

- *Raise DL based on available number of MBs and verify at least 4 times per year.*

Consensus Principles for DL

- *DL must be based on sound scientific principles.*
- *Detection procedures must account for variability and bias of method blank results.*
- *DL concepts must address false positive and negative errors, and qualitative identification for regulatory purposes.*
- *DL procedures must include ongoing demonstration.*
- *DL must account for temporal inter- and intra-laboratory variability.*
- *DL procedures must address matrix effects.*
- *Must adopt the definitions of L_C and L_D of ISO/IUPAC.*

Source: EPA-821-B-04-005, "Revised Assessment of Detection and Quantitation Approaches", (October 2004)

IUPAC Definitions for DL/QL

- *In his classic work on DL/QL in 1968, Dr. Lloyd Currie of NIST called for terminology standardization and defined:*
  - ***Critical Level (L_C)***
  - ***Detection Limit (L_D)***
  - ***Determination Limit / Quantification Limit (L_Q)***
- *Recommended by ACS Committee on Environmental Improvement in 1980 and adopted by IUPAC and ISO in 1995.*
- *However, IUPAC conventions do not provide practical ways to define and determine detection or quantitation limits.*

L_C/L_D Confusions

- *Dr. Lloyd Currie made the following statement:*

  "The meaning of 'detection limits' is perhaps clear to all, in a qualitative sense. That is, the detection limit is commonly accepted as the smallest amount or concentration of a particular substance that can be reliably detected in a given type of sample or medium by a specific measurement process. Within such a general definition, however, lurk many pitfalls in terminology, understanding, and formulation, that have led to several decades of miscommunication among scientists and between scientists and the public."

***Source: Chemometrics and Intelligent Laboratory Systems*, 37 (1997)**

Critical Level (L_c)

- *The measured value at which there is a small chance that the concentration in the sample is zero.*
- *The decision as to whether the substance has been detected is made by comparing the measurement result with the L_C.*
- *Measurements greater than the L_C have less than 1% change of being associated with a sample that does not contain the substance of interest.*

Detection Limit (L_D)

- *A true concentration that has a high probability of generating measured values greater than the L_C.*
- *Measurements on samples that contain concentrations equal to the L_D have a high probability of exceeding the L_C and are, therefore, unlikely to result in a decision that the substance is not detected in the sample.*
- *L_D is selected such that 99% of measurements on a sample containing this concentration are expected to be above the L_C.*

Currie's L_C and L_D

- *An alternative view of the L_C and L_D:*
  - ***L_C**: The lowest concentration for reliably reporting <u>detection</u> (FP = 1%).*
  - ***L_D**: The lowest concentration for reliably reporting <u>non-detect</u> (FN = 1%).*
- *If FP = FN = 1%, 99% of the measurements for samples not containing the analyte will be less than the L_C and 99% of the measurements with true concentration at the L_D will exceed the L_C.*

Source: DoD EDQW Detection and Quantitation Fact Sheet (9/2009)

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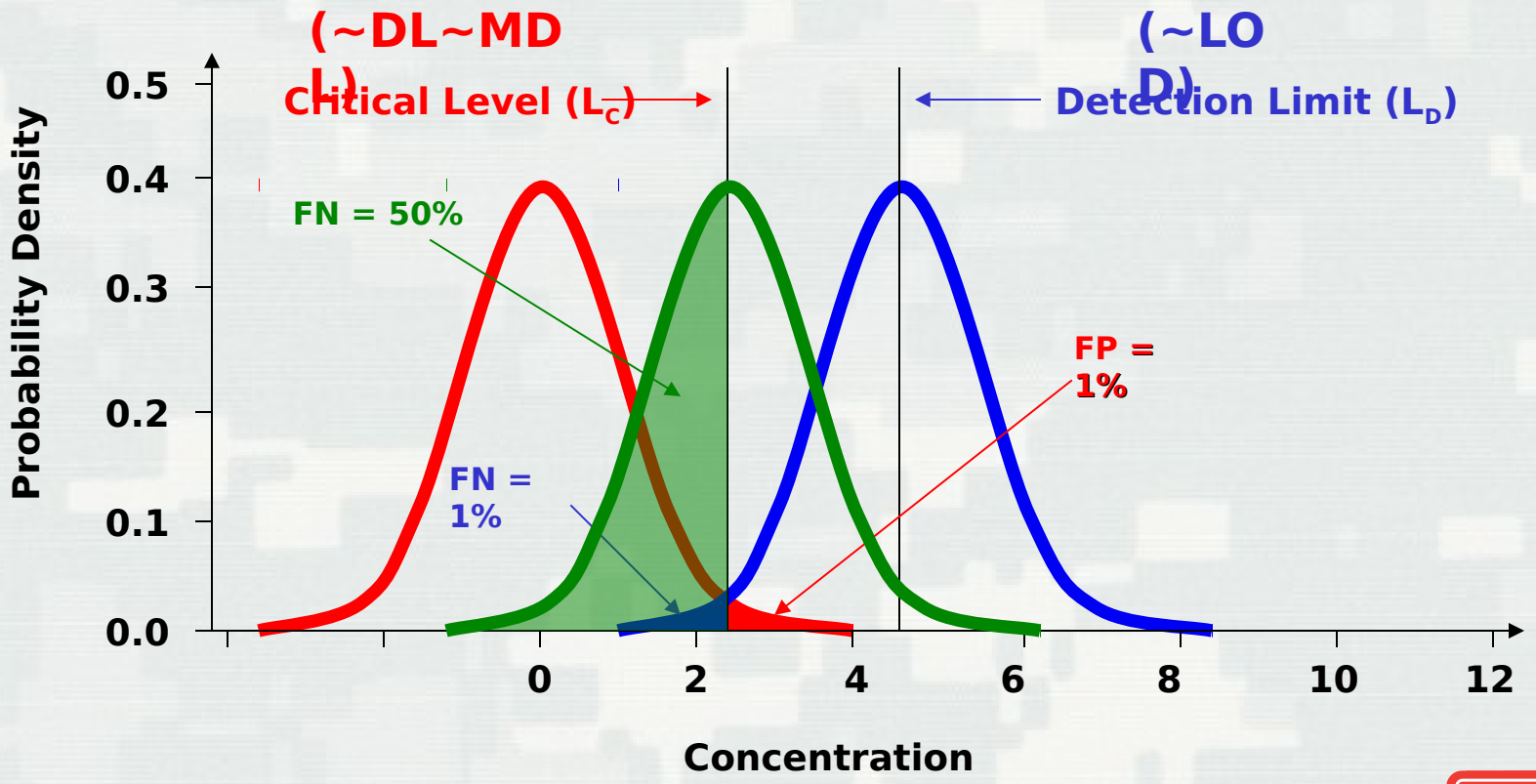
Graphic View of L_C and L_D



$$L_C = z_{1-\alpha}\sigma_0 \text{ and } L_D = L_C + z_{1-\beta}\sigma_D \approx 2 \times L_C \quad \text{, if } \sigma_0 \approx \sigma_D \text{ and } Z_{1-\alpha} = Z_{1-\beta}$$

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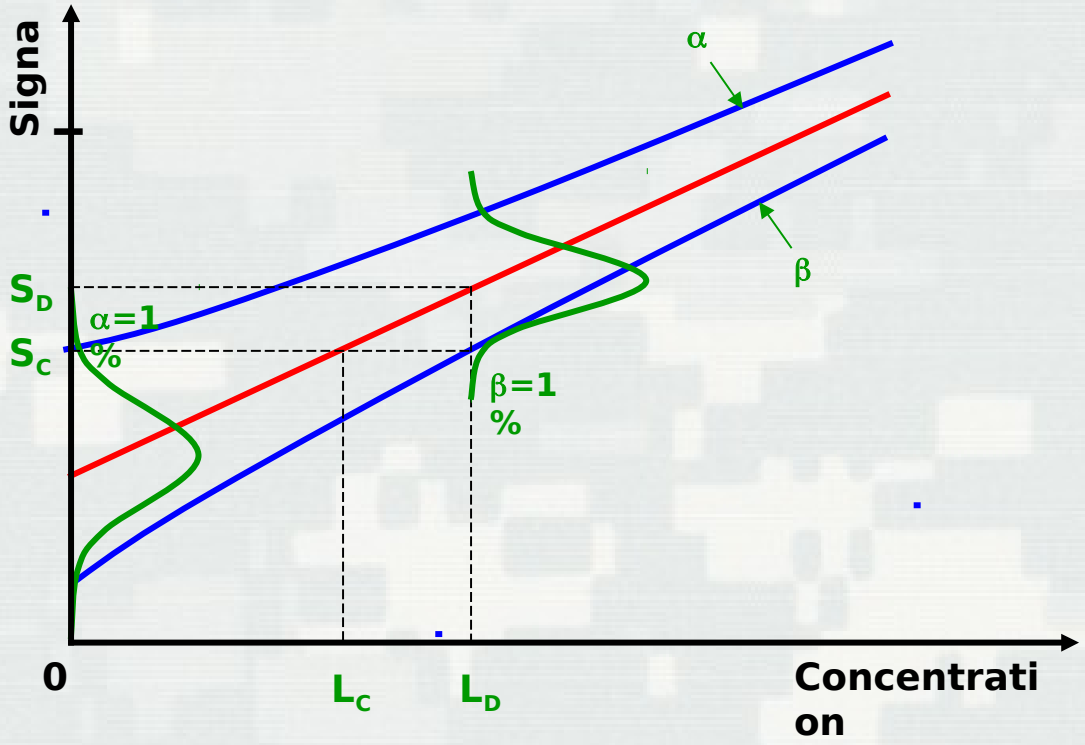
Graphic View of L_C and L_D

- *Hubaux and Vos: Calibration-based method for estimating L_C and L_D for linear calibration curves*



***Source: Analytical Chemistry*, 42 (1970)**

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L_C/L_D vs DL/LOD

Currie	ISO/ IUPAC	ACS	EPA	DoD V3	DoD V4.1
Critical Value	L_C	LOD	MDL	LOD	Detection Limit (DL)
Detection Limit	L_D	…	…	LOD Verification	LOD

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DoD QSM V4.1 Approach

- *Adopts IUPAC concepts of Critical Level (L_C) and Detection Limit (L_D).*
- *Replaces L_C and MDL with **DL** and L_D with **LOD**.*

Method Detection Limit: One way to establish a Limit of Detection, defined as the minimum concentration of a substance (an analyte) that can be measured and reported with 99% confidence that the analyte concentration is greater than zero and is determined from analysis of a sample in a given matrix containing the analyte.

Method Detection Limit (MDL) (Clarification): The MDL is one way to establish a Detection Limit, not a Limit of Detection.

A DoD "Detection Limit", not an IUPAC "Detection Limit (L_D)"

Limit of Detection (LOD): An estimate of the minimum amount of a substance that an analytical process can reliably detect. An LOD is analyte- and matrix-specific and may be laboratory-dependent.

Limit of Detection (Clarification): The smallest amount or concentration of a substance that must be present in a sample in order to be detected at a high level of confidence (99%). At the LOD, the false negative rate (Type II error) is 1%.

DoD QSM V4.1 Approach

- *Box 25: A laboratory shall determine and verify method sensitivity, precision, and bias in each quality system matrix of concern.*
- *Empirically determine DL with scientifically valid and legally defensible method – per 1996 Public Law 104-113 (15 USC 3701), National Technology Transfer and Advancement Act, which directs Federal agencies to increase their use of voluntary consensus standards.*
  - *Non-Censored Methods, e.g., ICP*
  - *Censored Method, e.g., GC, GC/MS*
- *Quarterly verify LOD.*

DoD QSM V4.1 Guidance

- *Box D-13:* ***DL ~ L_C ~ MDL*** *and* ***LOD ~ L_D ~ 2 × MDL****.*
- *Use scientifically valid and documented procedure to establish a DL for each suite of analyte-matrix-method.*
- *Immediately establish the LOD by spiking a quality system matrix at approximately 2 – 3× DL for single-analyte standards or 2 – 4× DL for multi-analyte standards.*
- *S/N ≥ 3 and the results meet analyte ID requirements.*
- ***LOD = [Spike Concentration]***
- *Verify the LOD quarterly.*
- *If verification fails, repeat DL determination and LOD verification at a higher concentration, or perform and pass two consecutive LOD verifications at a higher concentration.*

  LOD = [Higher Spike Concentration]
- *DoD Detection and Quantitation Fact Sheet:*

  https://www.denix.osd.mil/portal/page/portal/EDQW

DoD QSM V4.1 Applications

- *Box 25: Verify method sensitivity with LOD verification.*
- *Box 47: Report non-detect analytes as "< LOD" or "LOD U", adjusted for sample size, %moisture, and dilution or*

(Guidance) *Example: Detection limit (DL) = 2, Limit of Detection (LOD) = 4, Limit of Quantitation (LOQ) = 15, sample is undiluted. **Reporting Limit (RL) = 20.**

Sample #1: Analytical result: Not detected; Reported result: <4 U

Sample #2: Analytical result: 2; Reported result: 2 J

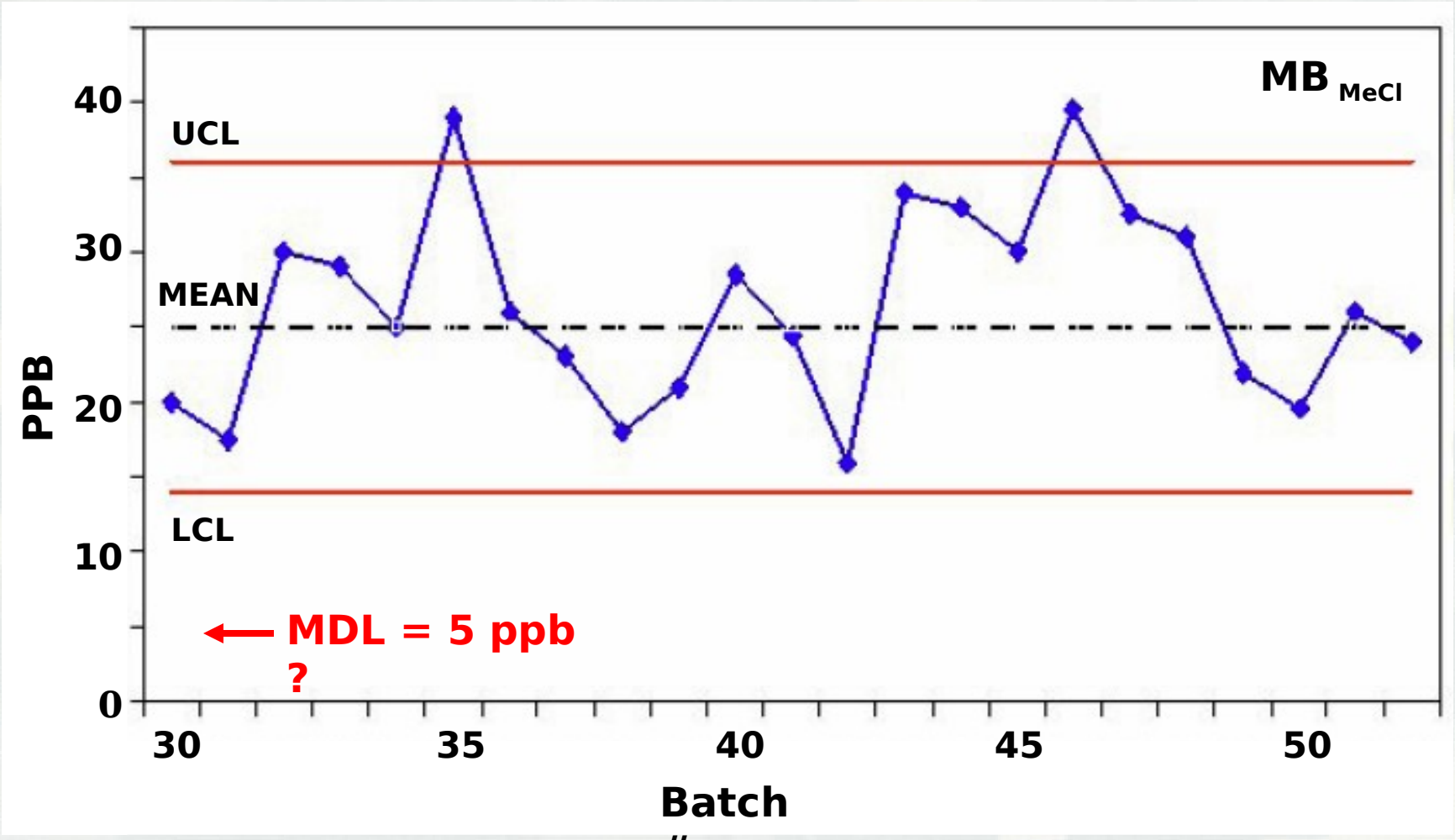
Sample #3: Analytical result: 10; Reported result: 10 J

Sample #4: Analytical result: 15; Reported result: 15

- *Box D-1: If any blanks fail, reprocess affected samples, unless sample concentration < LOD.*
- *Table F-1: Calibration Blank ≤ LOD.*
- *Table F-3: Confirm target analyte if concentration > LOD.*
- *Table F-7: All* [[non-spiked analyte]] *in ICS-A < LOD.*

*** AFCEE ERPIMS practically complies with the DoD QSM V4.1.**

Common Deficiencies



Common Deficiencies

- *Improper calculation of IDL based on arithmetic mean of 3 standard deviations.*

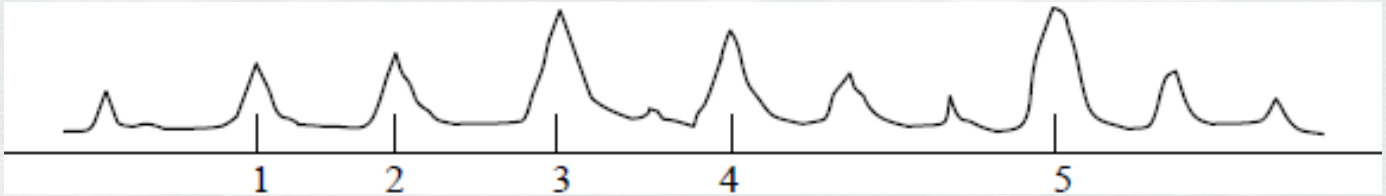
$$\sigma_{pooled} \neq \frac{\sigma_1 + \sigma_2 + \sigma_3}{3}$$

$$\sigma_{pooled} = \sqrt{\frac{(n_1 - 1) \times \sigma_1^2 + (n_2 - 1) \times \sigma_2^2 + (n_3 - 1) \times \sigma_3^2}{(n_1 - 1) + (n_2 - 1) + (n_3 - 1)}}$$

- *Aroclor DL is not properly calculated and Aroclor identification is not performed.*

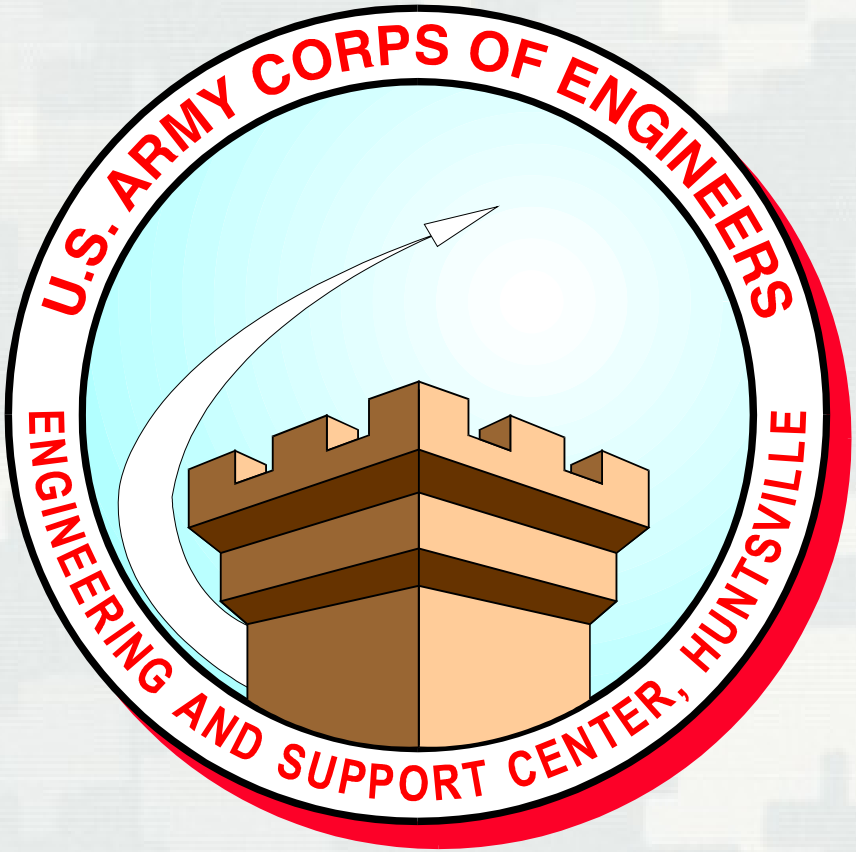
Common Deficiencies

- *DL for multi-component analytes is questionable.*



  - ***Method A**: Based on <u>mean concentration</u>.*
    Determine concentrations of 7 replicates based on mean concentration of 5 selected peaks and calculate DL based on standard deviation of 7 replicates.
  - ***Method B**: Based on <u>mean DL</u>.*
    Determine DLs of 5 selected peaks based on 7 replicates and calculate MDL based on arithmetic mean of 5 DLs.
  - ***Method C**: Based on <u>pooled standard deviation</u>.*
    Determine standard deviations of 5 selected peaks based on 7 replicates and calculate DL based on pooled standard deviations.

Questions?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Quantitation Limits

EQL PQL Determination Limit

RQL

Quantification Lim

MQ

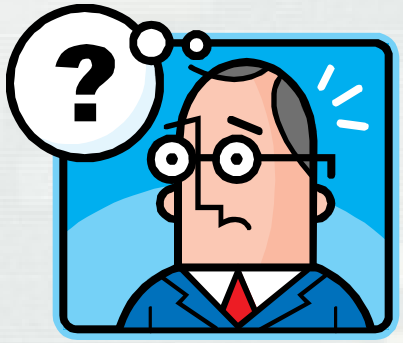
L_Q

LOQ

SQL

LCMRL

ML



AML

MRL

MQL

LRL

CMQL

RL

IQE WQE CRQL

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Example Definitions of QL

- *Minimum Level of Quantitation (**ML**): The minimum level at which the entire analytical system must give a recognizable signal and acceptable calibration point for the analyte.*

  - USEPA OW 40 CFR 136 methods

- *Practical Quantitation Limit (**PQL**): The lowest concentration of an analyte that can be reliably measured within specified limits of precision and accuracy during routine laboratory operation conditions.*

  - USEPA OW 52 FR 25690 July 1987

- *Estimated Quantitation Limit (**EQL**): The lowest concentration that can be reliably achieved within specified limits of precision and accuracy during routine laboratory operating conditions. The EQL is generally 5 to 10 times the MDL. For many analytes the EQL is selected as the lowest non-zero standard in the calibration curve.*

  - USEPA OSW SW-846

- *Method Quantitation Limit (**MQL**): The lowest amount of an analyte in a sample that can be quantitatively determined with stated, acceptable precision and accuracy under stated analytical conditions.*

  - International Conference on Harmonization (ICH) Harmonised Tripartite Guideline

Criticisms of Minimum Level of Quantitation (ML)

1. *Determined based solely on a measure of precision and not account for bias.*
2. *Fails to achieve a 10% precision.*
3. *Based on a multiple of the estimated standard deviation, which is assumed to be constant in the region of detection and quantitation.*
4. *Does not account for interlaboratory and temporal intralaboratory variability.*

Source: FACDQ (9/05)

Common Determination Procedures

- *Professional judgment*
- *Multiples of detection limit*
- *Lowest calibration standard*
- *Empirical procedures*
- *Lowest Concentration Minimum Reporting Level (LCMRL)*

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Professional Judgment

- *Based on historical QLs*
- *Based on EPA PE study data*
- *Based on arbitrary RSD*
- *Questionable data quality*

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Multiples of Detection Limits

- *LOQ = 10 × SD = 3.3 × LOD*
- *MQL = 5 ~ 10 × MDL, but never < 3 × MDL*
- *Arbitrarily defined or determined*
- *Questionable precision and bias*

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Lowest Calibration Standard

- *QL = Lowest calibration standard*
- *Sample preparation not taken into account*
- *QL depends on calibration techniques*
- *Questionable precision and bias*

Empirical Determination

- *Repetitive measurements at concentrations close to QL*
- *Based on the minimum concentration giving acceptable precision and bias*
- *Lacking standard procedures*
- *Expensive*

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LCMRL (Lowest Concentration Minimum Reporting Level)

- *EPA procedure for single-laboratory LCMRL and MRL (POL) of UCMR*
- *Lowest concentration that future recovery will fall within specified recovery range and confidence*
- *Based on linear regression and prediction intervals for next observation*
- *Complicated and expensive*

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Consensus Principles for QL

- *QL must be based on sound scientific principles.*
- *QL concepts must address precision, bias, and qualitative identification for regulatory purposes.*
- *DoD requires ongoing verifications for QL.*
- *QL must account for temporal inter- and intra-laboratory variability.*
- *QL procedures must address matrix effects.*
- *QL must adopt the definitions of L_C, L_D, and L_Q of ISO/IUPAC.*

Source: EPA-821-B-04-005 (2004)

Currie's Definitions for QL

- *Currie defined "Determination Limit (later Quantification Limit)" as the "performance characteristics that mark the ability of a chemical measurement process to adequately 'quantify' an analyte".*
- *Quantification limits "serve as benchmarks that indicate whether the chemical measurement process can adequately meet the measurement needs. The ability to quantify is generally expressed in terms of the signal or analyte value that will produce estimates having a specified relative standard deviation commonly 10%."*
- *From a statistical perspective, any measured value, along with knowledge of the precision of the measurement, is useful.*

DoD QSM V4.1 Approach

- *Definition:*

Limits of Quantitation (LOQ): The minimum levels, concentrations, or quantities of a target variable (e.g., target analyte) that can be reported with a specified degree of confidence.

Limit of Quantitation (Clarification): The lowest concentration that produces a quantitative result within specified limits of precision and bias. For DoD projects, the LOQ shall be set at or above the concentration of the lowest initial calibration standard.

- *LOQ ≠ Reporting Limit (RL)*

Reporting Limit: A client-specified lowest concentration value that meets project requirements for quantitative data with known precision and bias for a specific analyte in a specific matrix.

- *LOQ ≠ Lowest Calibration Standard*
- *LOQ ≠ A Multiple of MDL*

DoD QSM V4.1 Approach

- *Box D-14: Laboratory must establish LOQ with known and documented precision and bias and must verify LOQ quarterly.*
  - *DoD QSM V4.1 does not specify the procedures and acceptance criteria for establishing and verifying LOQ.*
- *Box D-14: LOQ and associated precision and bias must meet project RL requirements and must be reported.*
- *Box D-14: LOQ must be within calibration range.*
- *A laboratory may establish LOQ based on any scientifically valid and documented procedures.*
  - *NELAC Standard Chapter 5, Appendix C.*
  - *Replicate analyses of blank spiked at various concentrations.*
  - *Estimated based on in-house QC data of detection limit and LCS.*

DoD QSM V4.1 Applications

- *Box 33: Establish Quantitation Range.*

Quantitation Range: The range of values in a calibration curve between the LOQ and the highest successfully analyzed initial calibration standard. The quantitation range lies within the calibration range.

- *Box 47: Report analyte concentrations quantified between the DL and LOQ as estimated values.*

(Guidance) *Example: Detection limit (DL) = 2, Limit of Detection (LOD) = 4, Limit of Quantitation (LOQ) = 15, sample is undiluted.

Reporting Limit (RL) = 20

Sample #1: Analytical result: Not detected; Reported result: <4 U

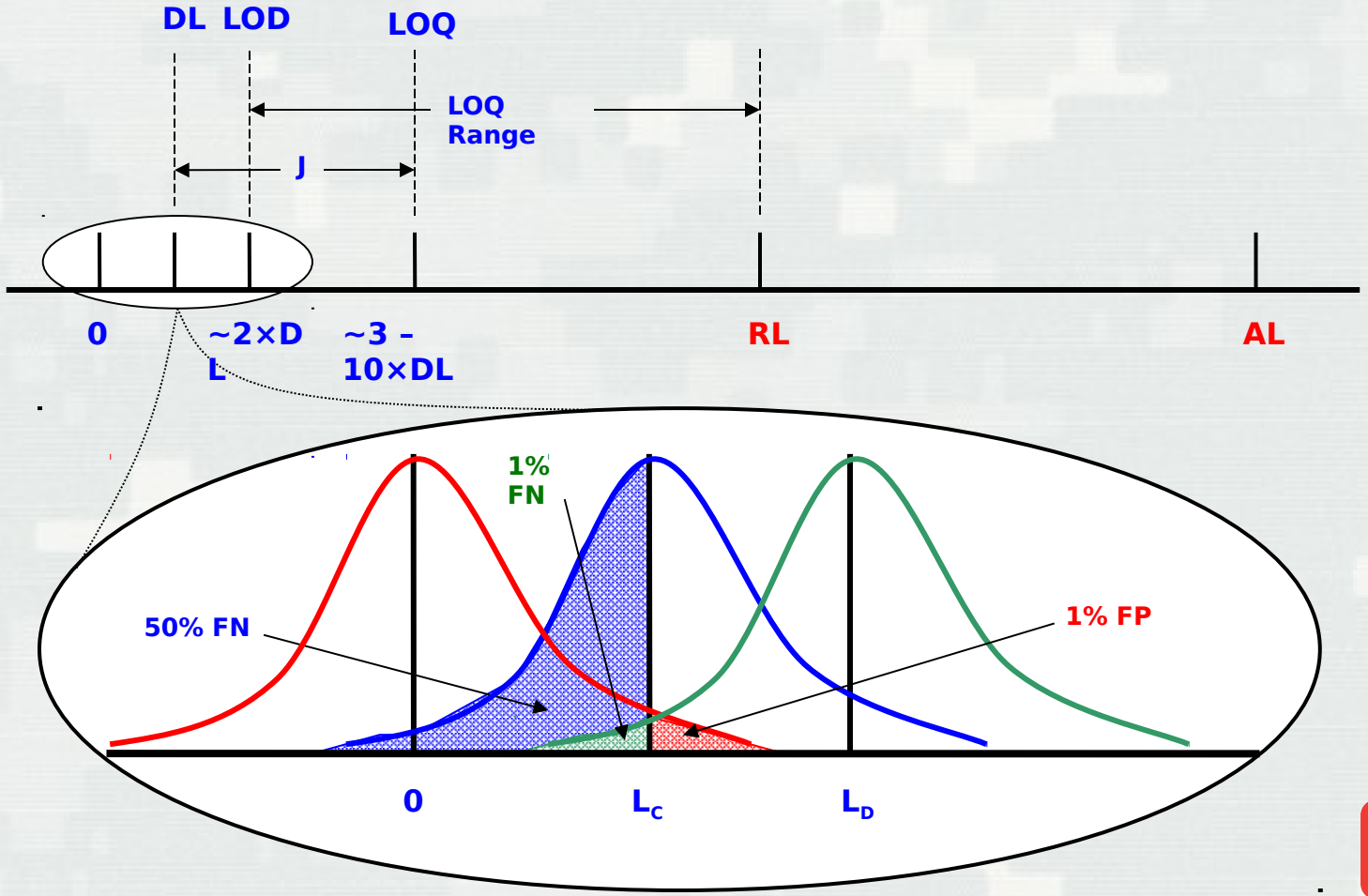
Sample #2: Analytical result: 2; Reported result: 2 J

Sample #3: Analytical result: 10; Reported result: 10 J

Sample #4: Analytical result: 15; Reported result: 15

- *Select qualified analytical methods and laboratories by comparing method and laboratory LOQ with project RL.*

Relationships among DL, LOD, LOQ, RL, and AL



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Proposed Procedure I

- *Determine LOQ based on precision and bias at various concentrations.*
- *Analyze quadruple blank spikes at LOQ to estimate precision and bias.*
- *Analyze LOQ verification sample(s) per batch to accumulate 20 – 30 data points for determination of precision and bias.*
- *Verify LOQ on a quarterly basis.*

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Proposed Procedure II

- *Determine LOQ based on precision and bias of laboratory QC samples.*
- *Adopt Rocke-Lorenzato Model for variance versus concentration.*
- *Set LOQ at the minimum concentration with stable RSD.*
- *Determine precision based on routine QC data of MDL/MB, and LCS.*
- *Verify LOQ on a quarterly basis.*

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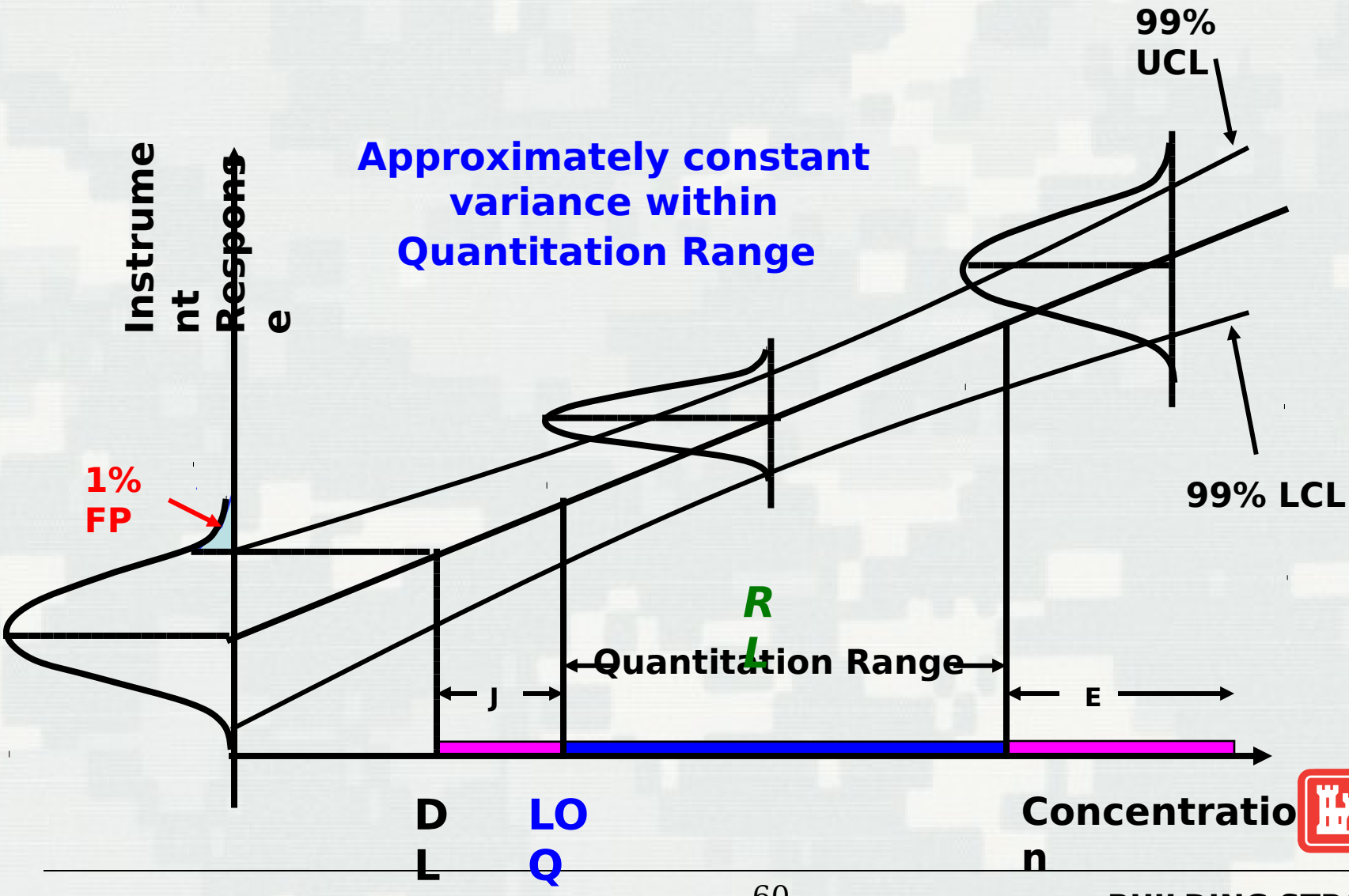
Measurement Uncertainty



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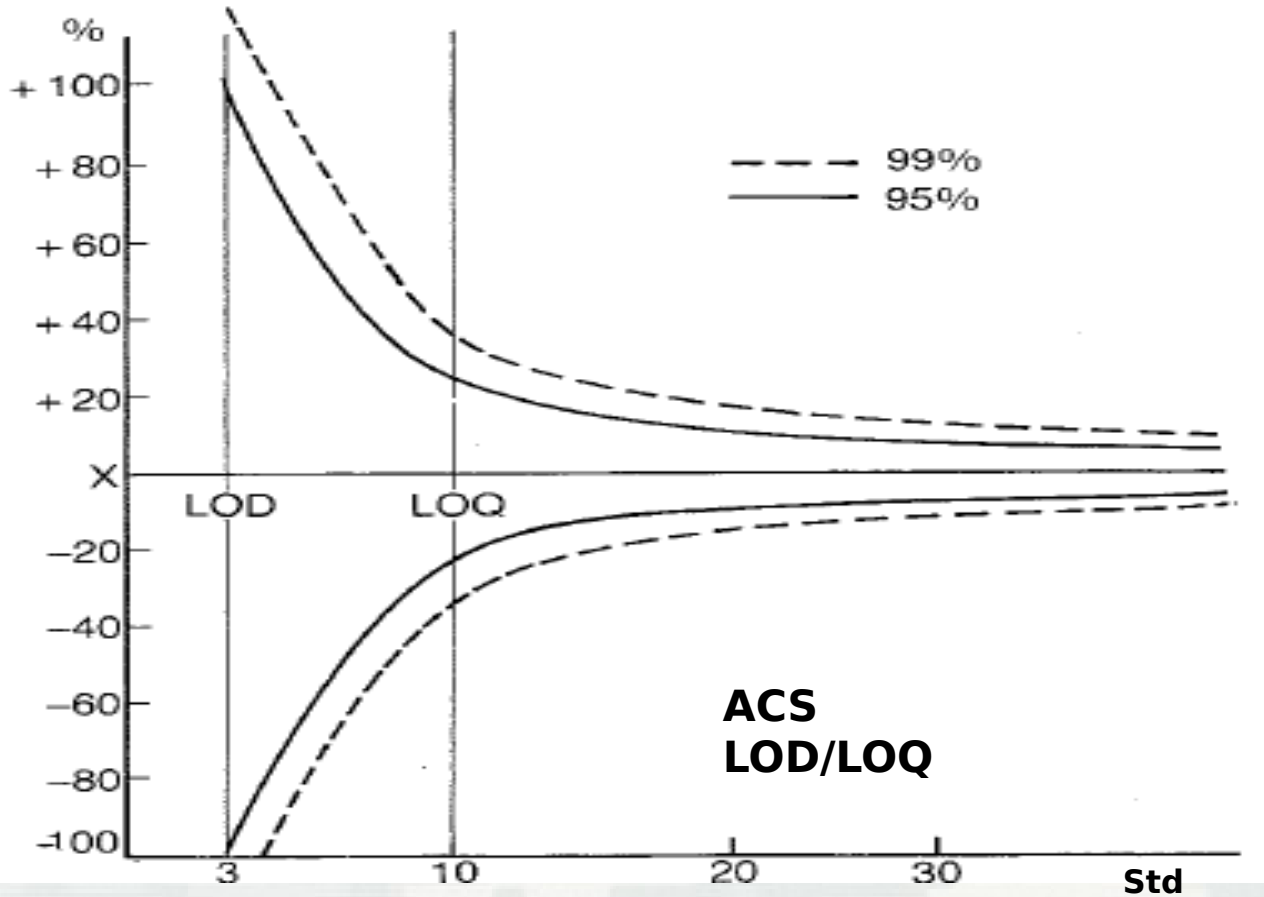
Measurement Uncertainty



Source: John K. Taylor, Quality Assurance of Chemical Measurements (1987)

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Two-Component Model for Measurement Uncertainty

- *Rocke-Lorenzato Model*

$$C = \varepsilon + \mu e^{\eta}$$

C: *measured concentration*

μ: *true concentration*

ε, η: *normally distributed with mean 0 and standard deviation* $\sigma_{\varepsilon}, \sigma_{\eta}$

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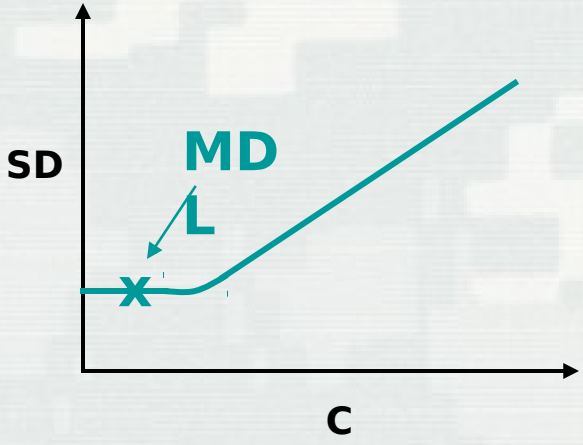
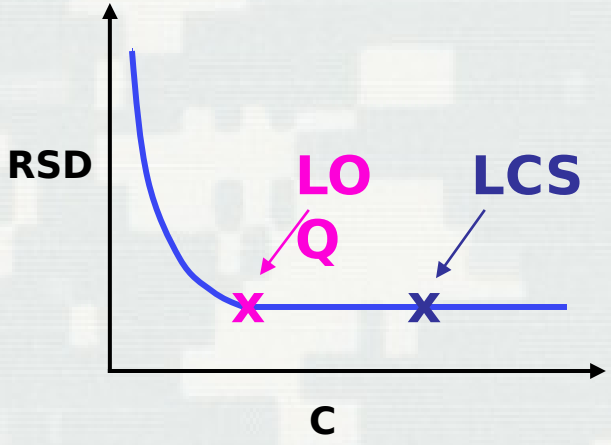
Two-Component Model for Measurement Uncertainty

- ***Rocke-Lorenzato Model***

$$\sigma_C = \sqrt{\sigma_\varepsilon^2 + \mu^2 e^{\sigma_\eta^2}(e^{\sigma_\eta^2} - 1)}$$

Variability is approximately constant near zero concentrations and increases proportionally with concentration at high concentrations.





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Estimated Uncertainty at C < LOQ

$U_{95\%}$ *Relative uncertainty at 95% confidence*

$$U_{95\%} = \pm \frac{t_{(n-1,.975)} \times \sigma_C}{C} \times 100\%$$

$$= \pm \frac{t_{(n-1,.975)} \times \sqrt{\sigma_\varepsilon^2 + \mu^2 e^{\sigma_\eta^2}(e^{\sigma_\eta^2} - 1)}}{C} \times 100\%$$

$$\approx \pm \frac{t_{(n-1,.975)} \times \sqrt{2} \times \sigma_\varepsilon}{N \times MDL} \times 100\%$$

$$= \pm \frac{t_{(n-1,.975)} \times \sqrt{2} \times \sigma_\varepsilon}{t_{(n-1,.99)} \times \sigma_\varepsilon} \times \frac{100\%}{N} \approx \pm \frac{100\%}{N}$$

for C *near* MDL *and* $C = N \times MDL$.

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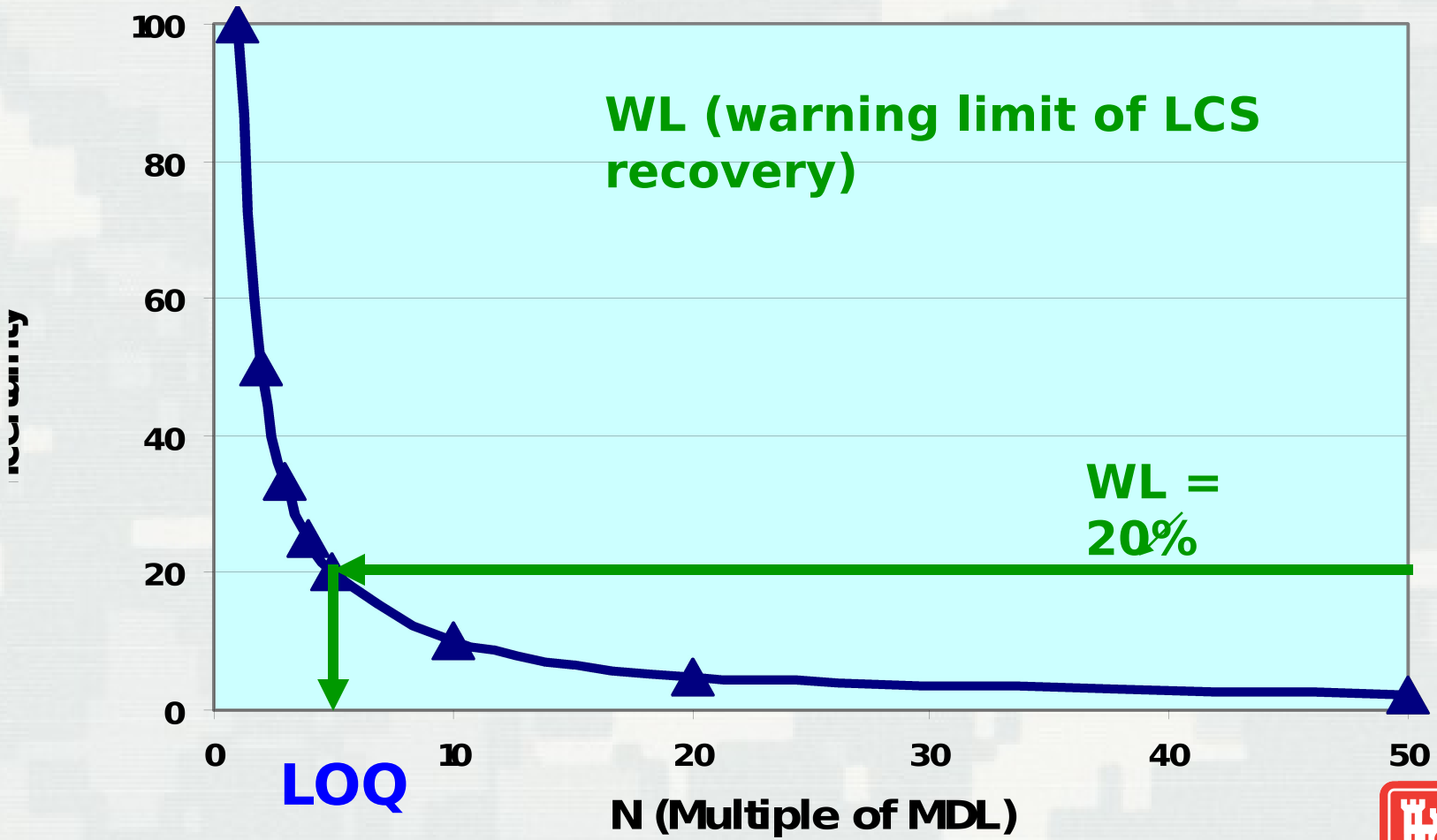
$U_{95\%}$ vs. Concentration



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LOQ Determination

- *LOQ is set at the minimum concentration where* $U_{95\%,\,MDL} = WL_{LCS}$

$$\frac{100\%}{N} = WL_{LCS} = \frac{t_{(n-1,.975)} \times \sigma_{LCS}}{\overline{C}_{LCS}} \approx 2 \times RSD_{LCS}$$

$$N = \frac{100\%}{WL_{LCS}} \approx \frac{100\%}{2 \times RSD_{LCS}}$$

LOQ = N × MDL ≈ N × DL

with the same P&B of LCS

Example

- ***MDL* = 1 ppb, CL_{LCS} = 60% – 120%, *LOQ* = ?**

$$RSD = \frac{120\% - 60\%}{6} = 10\%$$

$$WL_{LCS} = 2 \times RSD = 20\%$$

$$LOQ = N \times MDL = \frac{100\%}{WL_{LCS}} \times MDL$$

$$= \frac{100\%}{20\%} \times 1\,ppb = 5\,ppb$$

with RSD = 10% and %R = 90%

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Two-Component Model for Measurement Uncertainty

Analyte	Method	Spike Level	Mean Conc.	Mean (% Recovery)	SD Conc.	RSD (based on Mean)
1112-PCA	524.2	0.035				
1112-PCA	524.2	0.05				
1112-PCA	524.2	0.075				
1112-PCA	524.2	0.1				
1112-PCA	524.2	0.15	0.032	21.178	0.023	72.898
1112-PCA	524.2	0.2	0.090	44.886	0.020	22.297
1112-PCA	524.2	0.35	0.253	72.367	0.019	7.417
1112-PCA	524.2	0.5	0.416	83.143	0.013	3.211
1112-PCA	524.2	0.75	0.660	88.000	0.012	1.797
1112-PCA	524.2	1	0.830	82.986	0.035	4.185
1112-PCA	524.2	2	1.760	88.000	0.062	3.533
1112-PCA	524.2	5	4.239	84.771	0.132	3.104
1112-PCA	524.2	10	8.800	88.000	0.234	2.661
1112-PCA	524.2	20	16.729	83.643	0.486	2.902
1112-PCA	524.2	50	43.957	87.914	0.846	1.925
1112-PCA	524.2	100	94.543	94.543	2.625	2.776
1112-PCA	524.2	200	235.429	117.714	9.253	3.930

MDL = 0.05

(Source: EPA Episode 6000 Study)

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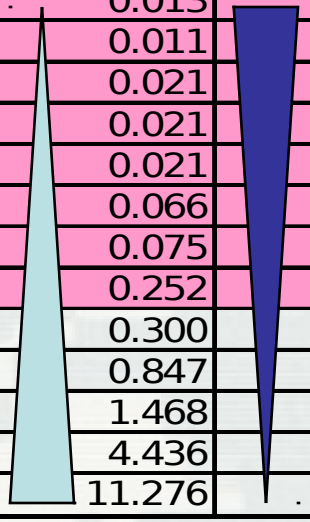
Two-Component Model for Measurement Uncertainty

Analyte	Method	Spike Level	Mean Conc.	Mean (% Recovery)	SD Conc.	RSD (based on Mean)
111-TCA	524.2	0.035				
111-TCA	524.2	0.05				
111-TCA	524.2	0.075				
111-TCA	524.2	0.1	0.146	146.000		
111-TCA	524.2	0.15	0.036	24.133	0.013	36.624
111-TCA	524.2	0.2	0.105	52.250	0.011	10.410
111-TCA	524.2	0.35	0.262	74.980	0.021	7.864
111-TCA	524.2	0.5	0.428	85.629	0.021	4.822
111-TCA	524.2	0.75	0.658	87.714	0.021	3.137
111-TCA	524.2	1	0.829	82.886	0.066	7.992
111-TCA	524.2	2	1.861	93.071	0.075	4.049
111-TCA	524.2	5	4.426	88.514	0.252	5.688
111-TCA	524.2	10	9.265	92.650	0.300	3.236
111-TCA	524.2	20	17.614	88.071	0.847	4.811
111-TCA	524.2	50	46.686	93.371	1.468	3.144
111-TCA	524.2	100	98.729	98.729	4.436	4.494
111-TCA	524.2	200	220.857	110.429	11.276	5.105



(Source: EPA Episode 6000 Study)

MDL = 0.06

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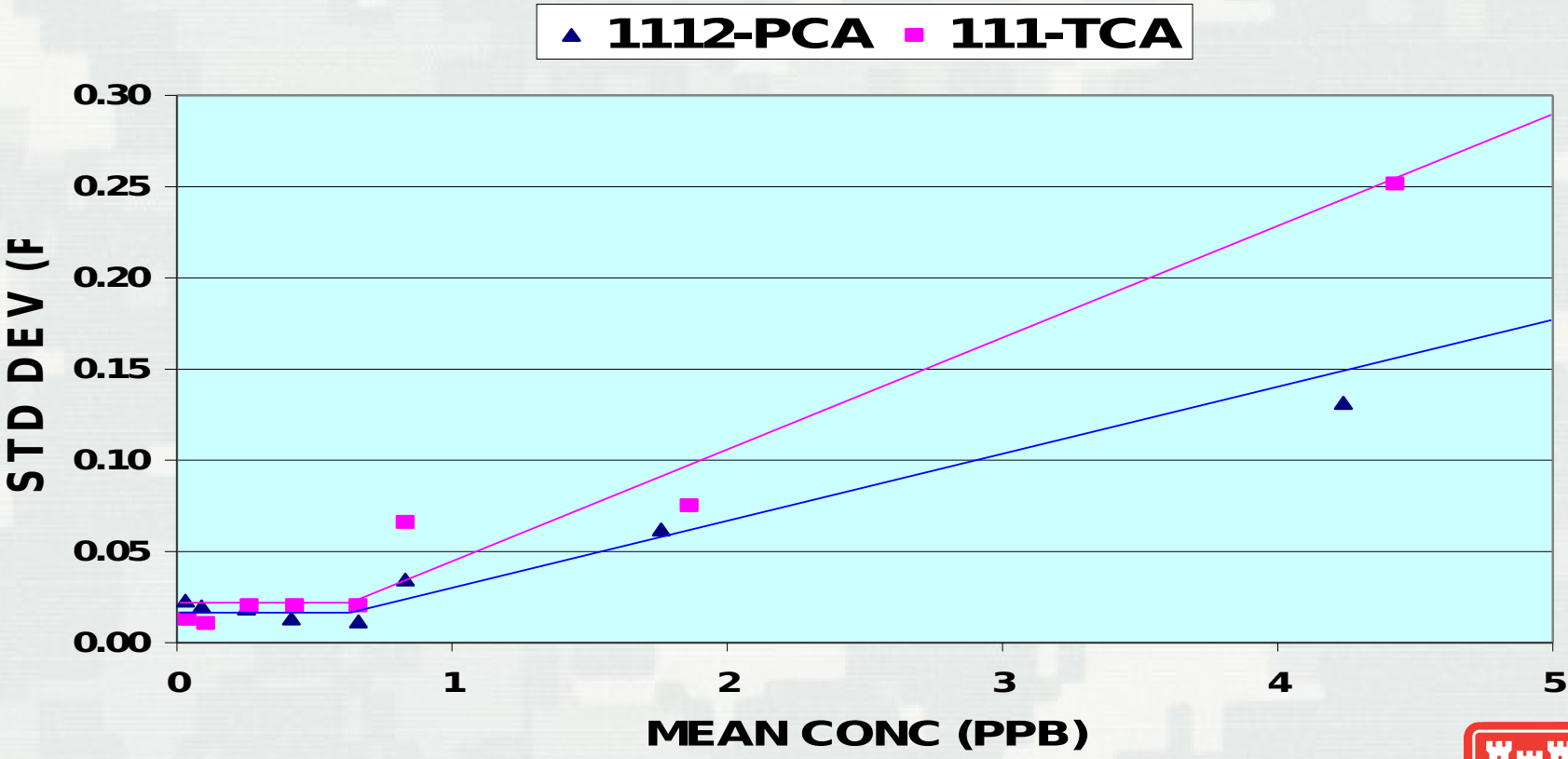
Two-Component Model for Measurement Uncertainty



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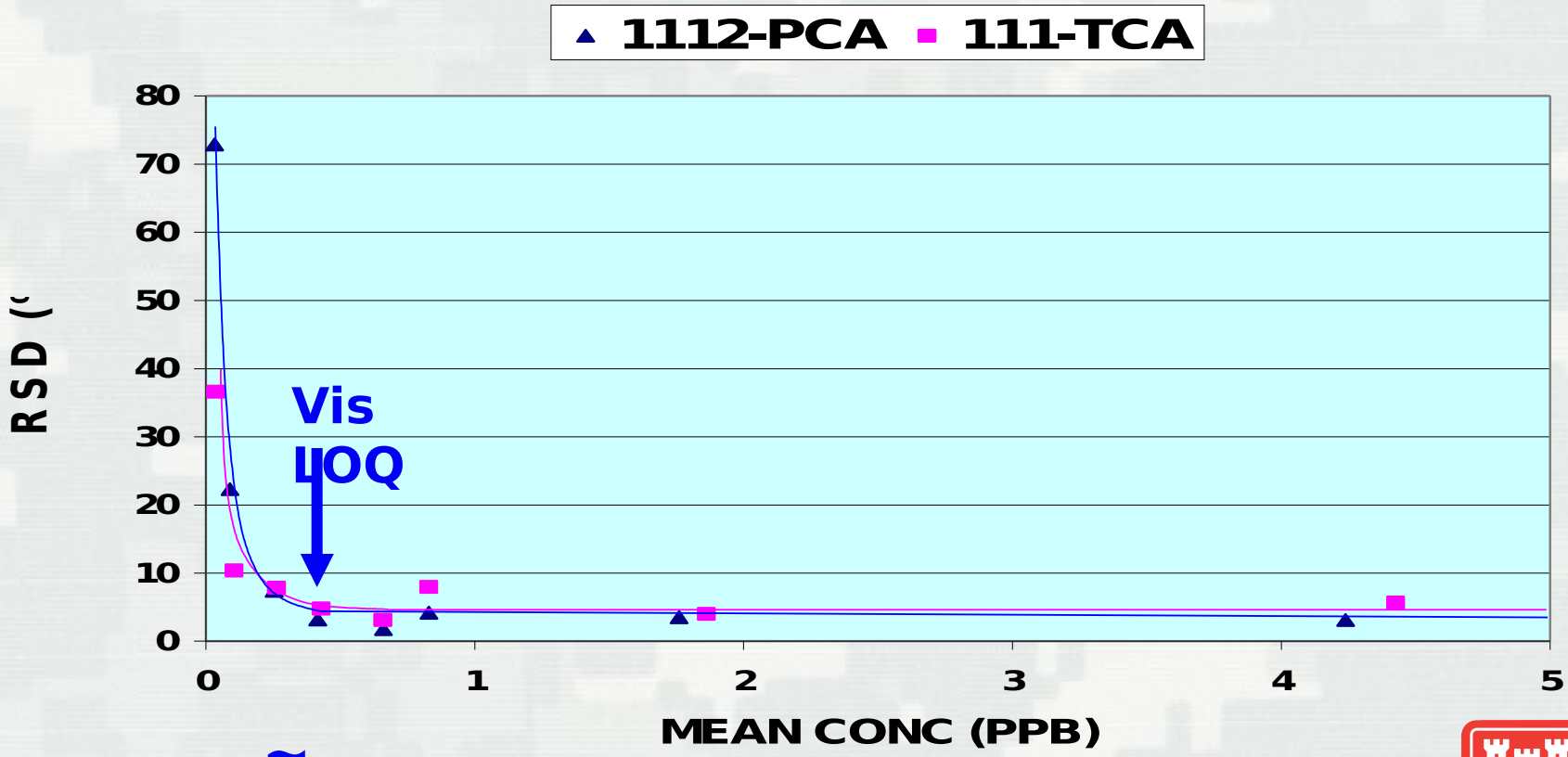
Two-Component Model for Measurement Uncertainty



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Example: 1112-PCA

MDL = t × s = 3.143 × 0.017 = 0.05 ppb

LOQ = 3 × MDL = 0.15 ppb

LOQ = 5 × MDL = 0.25 ppb

LOQ = 10 × MDL = 0.50 ppb

Unknown

Which one is a reliable LOQ?

RSD_{LCS} = 3.0% ⇒ 2 × RSD_{LCS} = 6.0%

LOQ = (100% / 6%) × MDL = 0.83 ppb

with RSD = 3% and %R = 91%

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Example: 111-TCA

MDL = t × s = 3.143 × 0.018 = 0.06 ppb

LOQ = 3 × MDL = 0.18 ppb

LOQ = 5 × MDL = 0.30 ppb

LOQ = 10 × MDL = 0.60 ppb

Unknown

Which one is a reliable LOQ?

RSD_{LCS} = 5% ⇒ 2 × RSD_{LCS} = 10%

LOQ = (100% / 10%) × MDL = 0.60 ppb

with RSD = 5% and %R = 93%

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Comparison of MQLs

	PCA	TCA
MDL	0.05	0.06
CL_{LCS} 15%	± 9%	±
3 × MDL	0.15	0.18
5 × MDL	0.25	0.30
10 × MDL	0.50	0.60
EPA ML	0.2	0.2
ISO LOQ	0.18	0.10
Calc LOQ (RSD/%R) (5%/93%)	0.83 (3%/91%)	0.60

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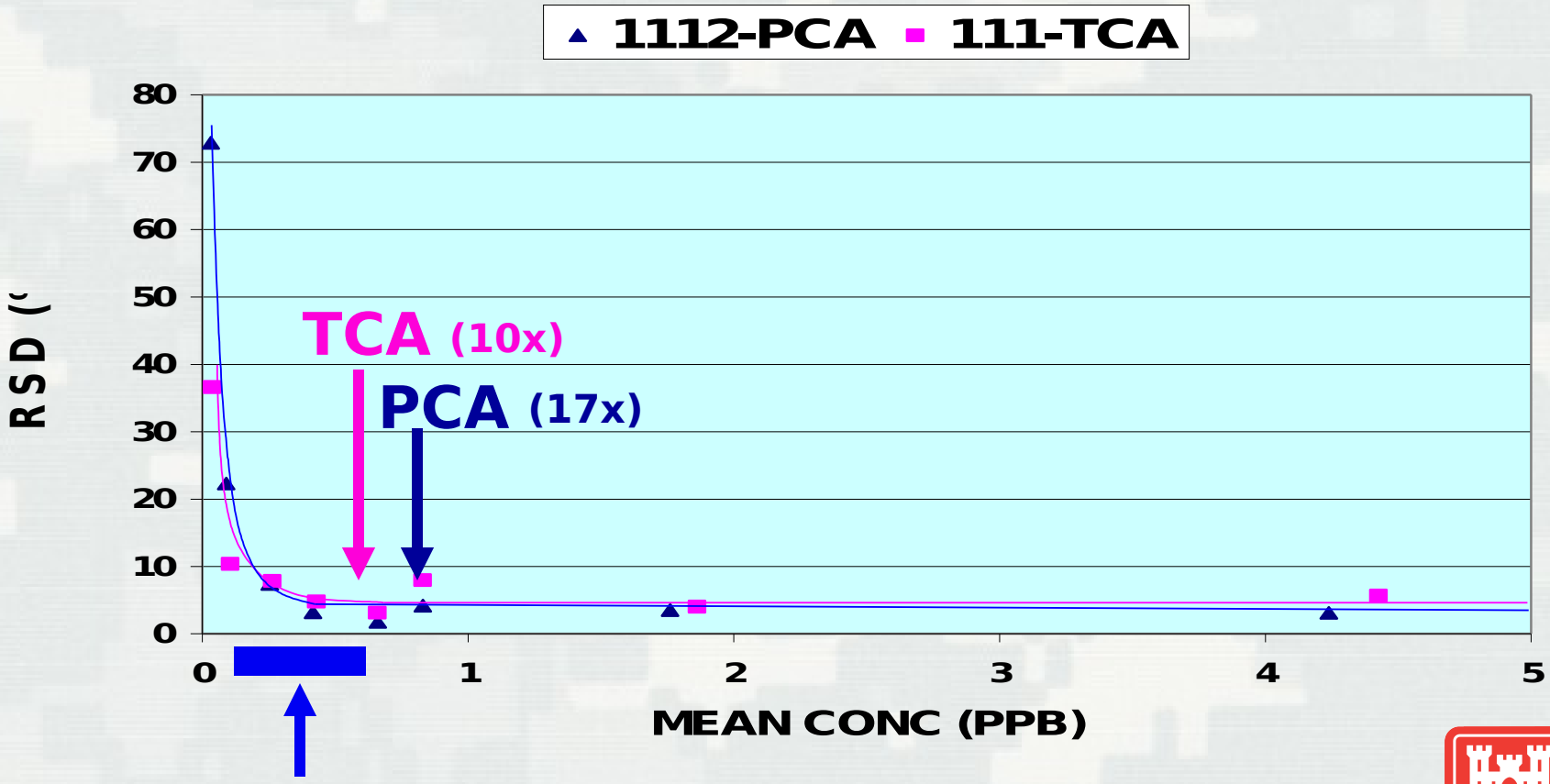
Two-Component Model for Measurement Uncertainty



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MQL Calculator

ANALYTE	4-Nitrophenol	4-Nitrophenol
MATRIX	water	water
METHODS	3520C/8270C	3510C/8270C
MDL (ppb)	10	10
LCS LCL (%)	70	40
LCS UCL (%)	130	160
MQL (ppb)	50	25
PRECISION (RSD)	10	20
BIAS (%R)	100	100

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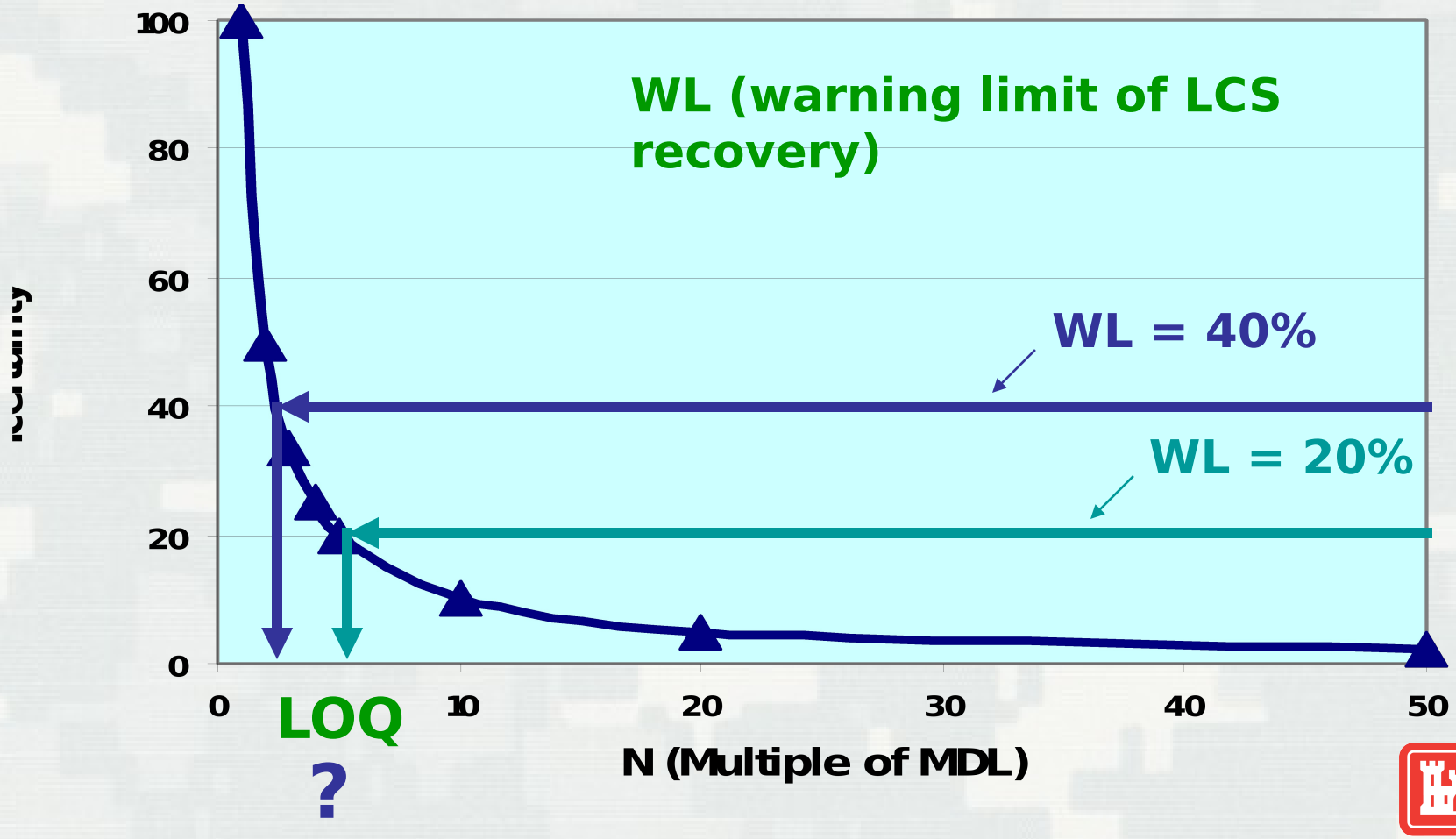
LOQ vs RSD_{LCS}



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LOQ Protocol

- *LOQ shall be reported and used with reliable precision and bias. LOQ without precision and bias is of no or limited use.*
- *Precision and bias of analytes with C ≥ LOQ in a blank matrix would be similar to the LCS'.*
- *LOQ ≥ LOD with known and documented precision and bias, and meet with project MQO.*

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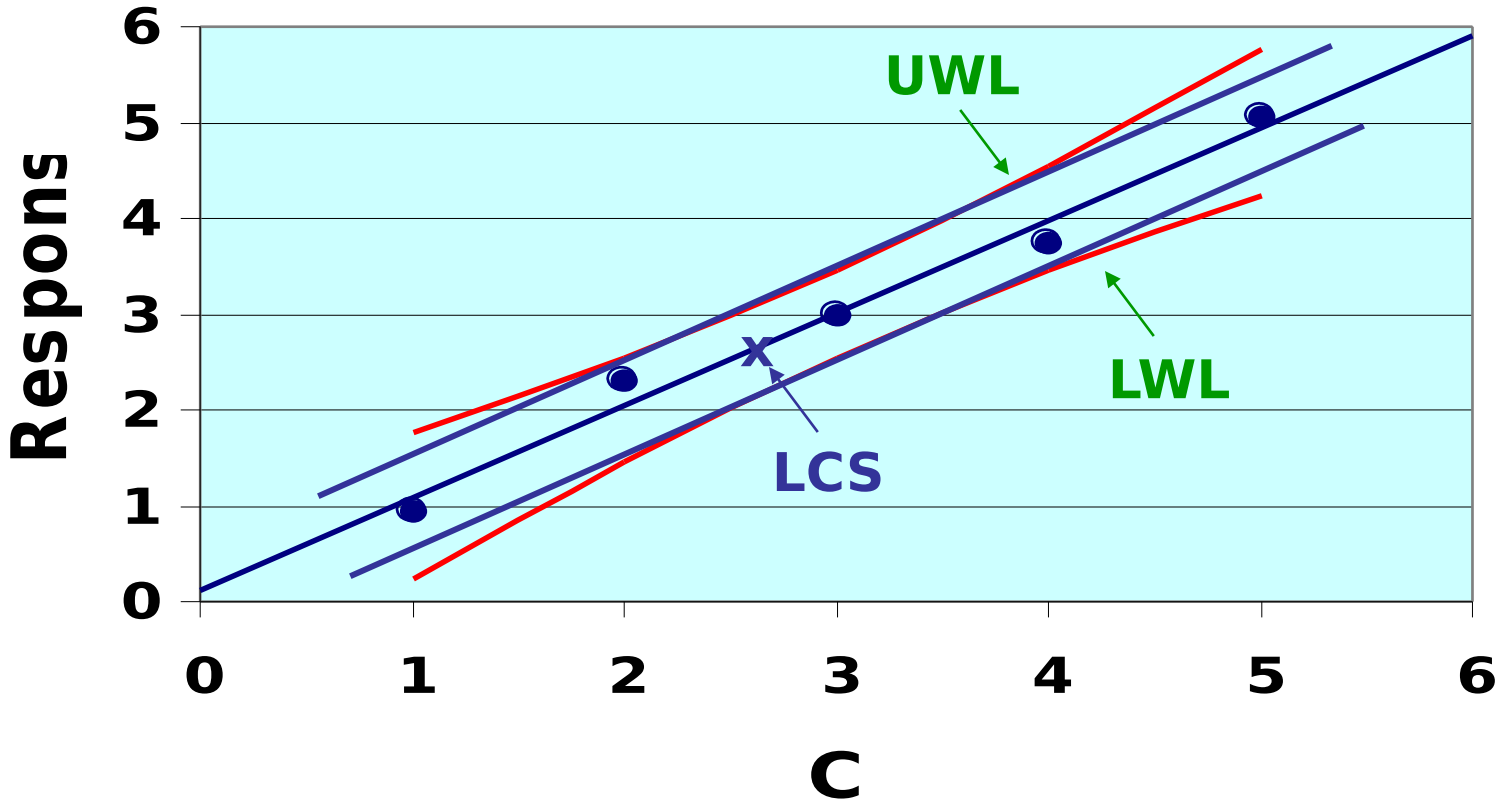
Accuracy of LOQ Procedure

- ***Mandel-Linnig Hyperbola***



Assumption 1: Constant RSD at C ≥ LOQ

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High bias LOQ with low bias uncertainty

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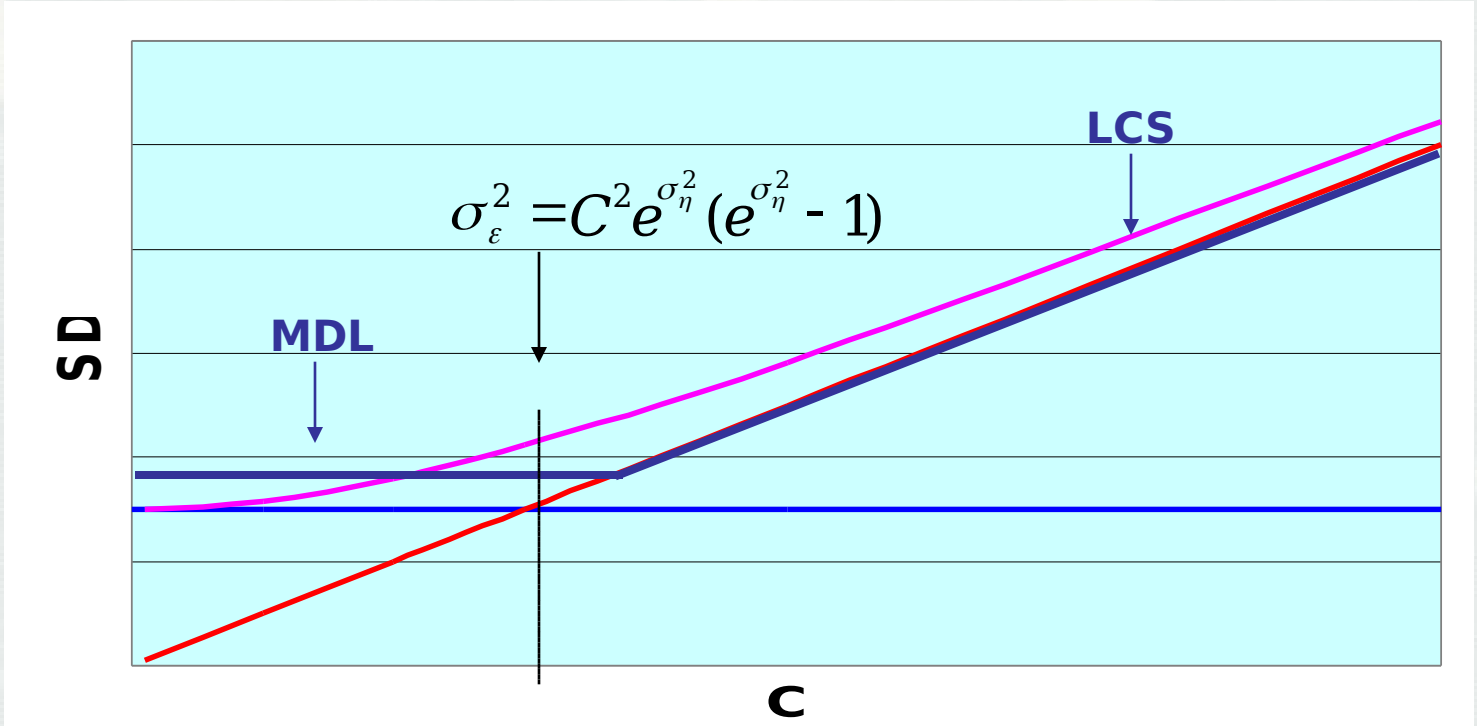
Accuracy of LOQ Procedure

- ***Rocke and Lorenzato Model***

$$\sigma_C = \sqrt{\sigma_\varepsilon^2 + C^2 e^{\sigma_\eta^2}(e^{\sigma_\eta^2} - 1)} \approx \sqrt{2} \times \sigma_\varepsilon \quad for\ small\ C$$



Assumption 2: Constant SD at C < LOQ

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High bias MQL with high bias uncertainty

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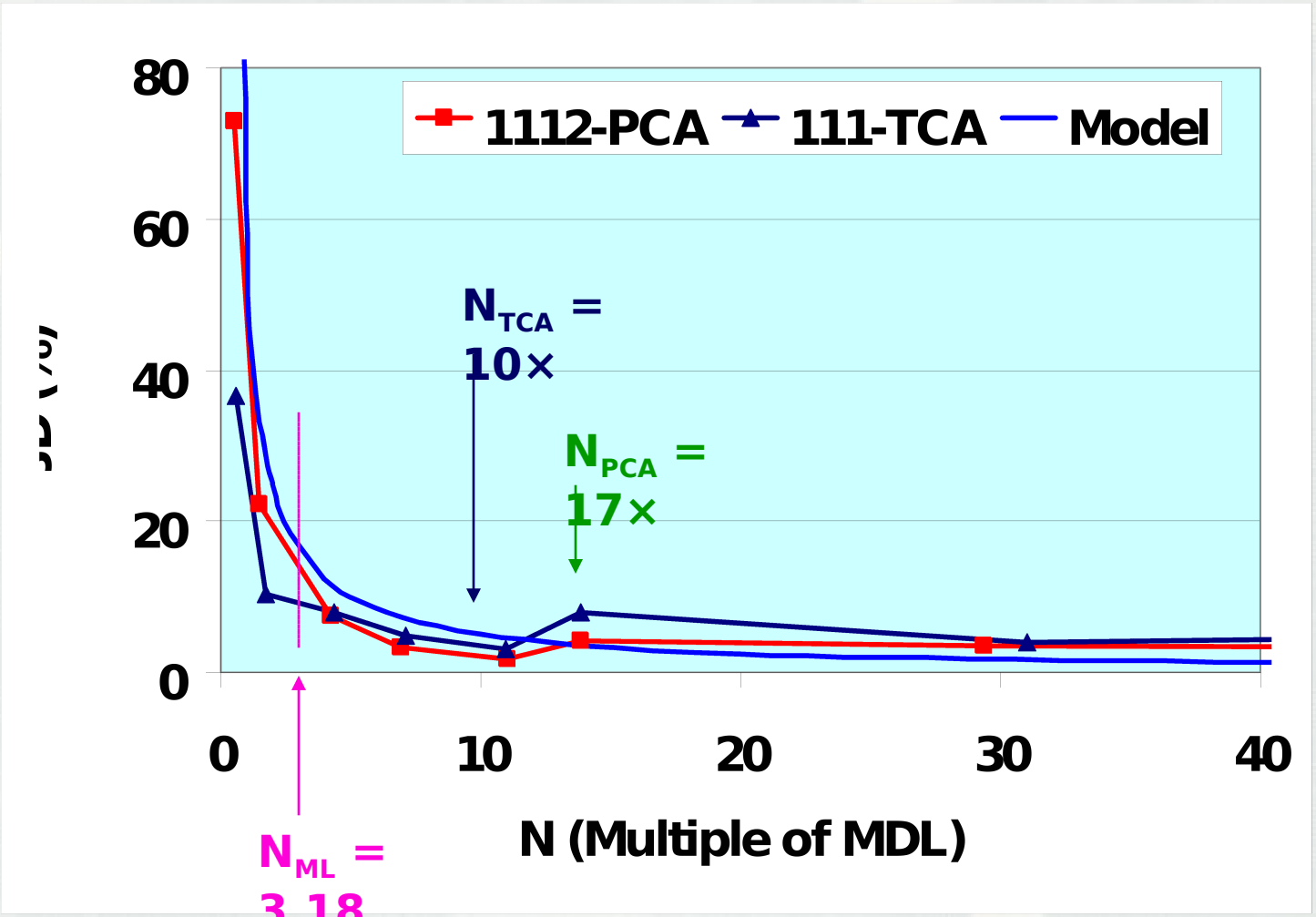
Accuracy of LOQ Procedure



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QC Issues

- *LOQ shall be verified on a routine basis*
- *MDL shall be properly determined*
- *LCS control charts shall be properly maintained*
- $U_{95\%,\,MDL}$ *may be replaced with* $U_{95\%,\,MB}$

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LOQ vs LCMRL

Method 521

Determination of Nitrosamines in Drinking Water by Solid Phase Extraction and Capillary Column Gas Chromatography with Large Volume Injection and Chemical Ionization Tandem Mass Spectrometry

Version 1.0, September, 2004
Document #: EPA/600/R-05/054

National Exposure Research Laboratory
Office of Research and Development, USEPA

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LOQ vs LCMRL

Table 1. Detection Limits and Lowest Concentration Minimum Reporting Levels [a, b]

Analyte	DL (ng/L)	LCMRL (ng/L)
NDMA	0.28	1.6
NMEA	0.28	1.5
NDEA	0.26	2.1
NPYR	0.35	1.4
NDPA	0.32	1.2
NPIP	0.66	1.4

a. DLs determination from LFBs fortified at 1.0 ng/L (n = 8).
b. LCMRLs determined from LFBs fortified at 1.0, 2.0, 3.0, and 4.0 ng/L (n = 5 or 6 at each concentration).

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LOQ vs LCMRL

Table 6. Precision and Accuracy Data Obtained from Fortified Reagent Water at Four Concentrations

Analyte	Fortified Conc 2.0 ng/L (n = 7)		Fortified Conc 4.0 ng/L (n = 6)		Fortified Conc 10.0 ng/L (n = 4)		Fortified Conc 20.0 ng/L (n = 6)	
	Accuracy (%R)	Precision (RSD)	Accuracy (%R)	Precision (RSD)	Accuracy (%R)	Precision (RSD)	Accuracy (%R)	Precision (RSD)
NDMA	94.7	12	92.7	11	88.7	3.8	89.5	7.8
NMEA	81.8	9.6	83.1	6.3	86.5	4.5	90.9	6.9
NDEA	84.6	9.0	92.0	14	87.5	9.1	95.6	11
NPYR	92.6	12	102	4.0	101	5.0	101	6.1
NDPA	81.7	8.0	87.6	7.3	97.0	10	87.1	7.7
NPIP	98.3	20	86.3	6.1	91.8	3.7	93.6	4.0

LOQ vs LCMRL

ANALYTE (Conc)	NDMA (2 ppt)	NDMA (4 ppt)	NDMA (10 ppt)	NDMA (20 ppt)	NDMA (pooled)
MATRIX	water	water	water	water	water
METHODS	3535/521	3535/521	3535/521	3535/521	3535/521
MDL (ppt)	0.28	0.28	0.28	0.28	0.28
LCS LCL (%)	131	126	100	113	113
LCS UCL (%)	59	60	77	66	71
LOQ (ppt)	1.2	1.3	3.7	1.8	2.0
PRECISION (RSD)	12	11	4	8	7
BIAS (%R)	95	93	89	90	92

Method 521: LCRML = 1.6 ppt with %R = 50 – 150% @ 99% confidence

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Summary

- *Simple, practical, and conservative procedure for determination of MQL.*
- *LOQ is determined based on in-house QC data.*
- *MDL and LCS studies shall be properly performed and documented.*
- *LOQ shall be verified on a routine basis.*
- *LOQ shall be reported with precision and bias.*

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Questionable MDL Study

Preparation Method: 3510C Date: 3/2/01 Analytical Method: 8270C
Date: 3/2/01

Analyte	Spike	R1	R2	R3	R4	R5	R6	R7	R8	Mean	Std.	MDL
	%REC	µg/L	µg/L	µg/L	µg/L	µg/L	µg/L	µg/L	µg/L	µg/L	Dev.	µg/L
	Mean/MDL Ratio											
Phenol	5	2.71	2.92	3.94	4.04	3.66	3.66	3.46	3.46	3.48	0.462	1.39	69.6	2.5
4-Chloroaniline	5	0.79	0.82	0.91	0.68	N.D.	1.44	N.D.	0.63	0.88	0.293	0.98	17.6	0.9
3-Nitroaniline	5	2.48	2.84	2.79	2.73	N.D.	N.D.	2.51	2.86	2.70	0.167	0.56	54.0	4.8
4-Nitroaniline	5	6.41	6.45	6.54	6.46	N.D.	N.D.	6.49	6.52	6.48	0.048	0.16	29.6	40.2
4-Nitrophenol	5	6.9	6.78	6.85	6.17	6.69	6.12	7.24	6.64	6.67	0.373	1.12	133.5	6.0
Pentachlorophenol	5	9.09	9.24	8.9	8.4	9.17	8.78	9.85	9.56	9.12	0.451	1.35	182.5	6.7
Pyrene	5	3.8	4.18	4.86	5.05	3.77	3.8	4.15	4.28	4.24	0.487	1.46	84.7	2.9

95% confidence interval for MDL: LCL = 0.64 MDL and UCL = 2.20 MDL

MDL = Standard Deviation × t factor (3.00 for 8- and 3.14 for 7-replicates)

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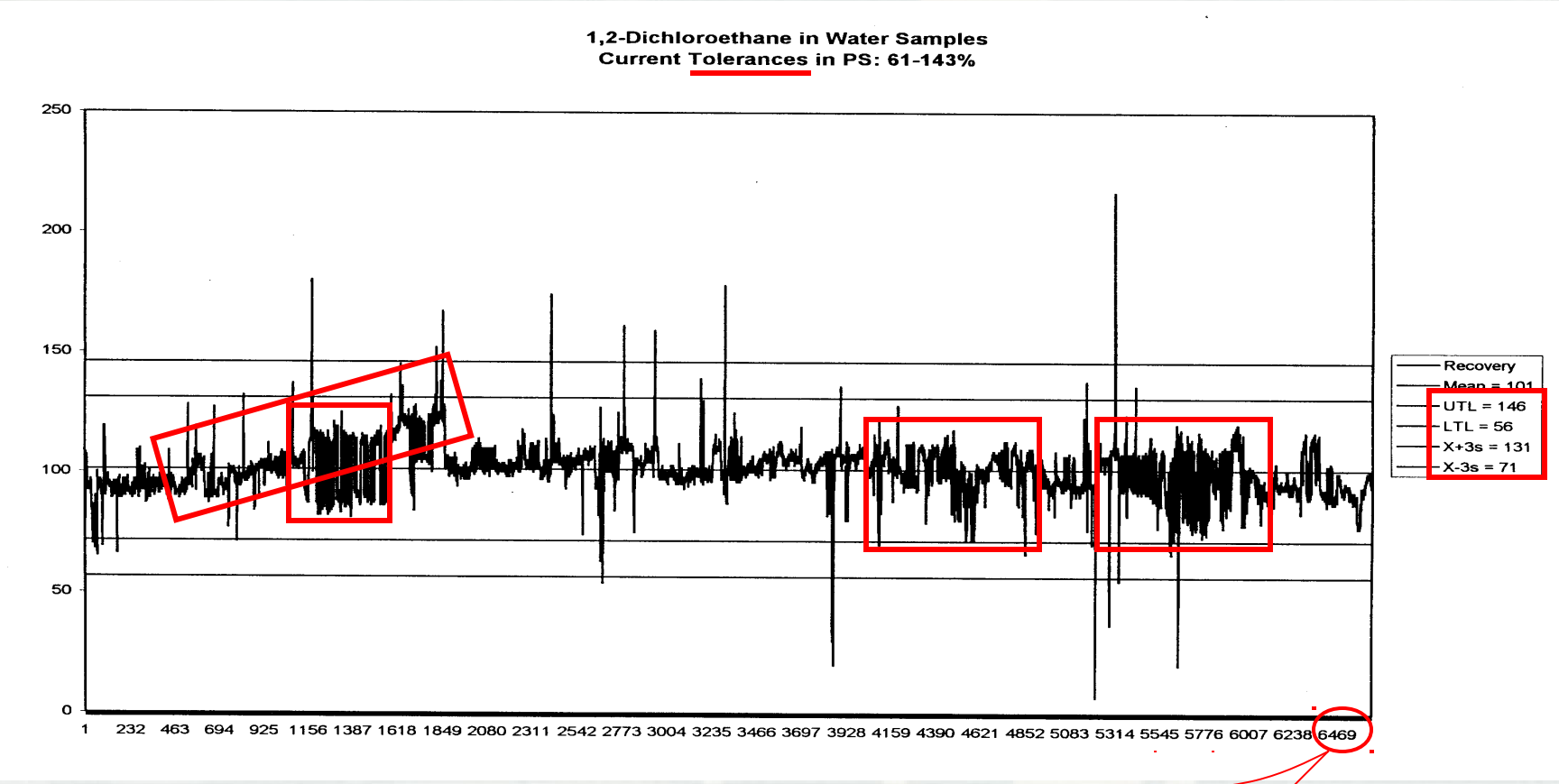
Laboratory Control Sample (LCS)

- *Use scientifically valid and documented procedures to establish LCS control limits.*
  - ► *Number of points*
  - ► *Treatment of outliers*
  - ► *Confidence, prediction, or tolerance intervals*
- *Verify reported LCS control limits with laboratory's in-house control charts.*

LCS Control Chart



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Common Deficiencies

- *No reliable precision and bias information associated with the LOQ*
- *No SOP for determination or verification of LOQ.*
- *LOQ = Lowest calibration standard*
- *Report non-detects as "< Reporting Limits", instead of "LOD U".*

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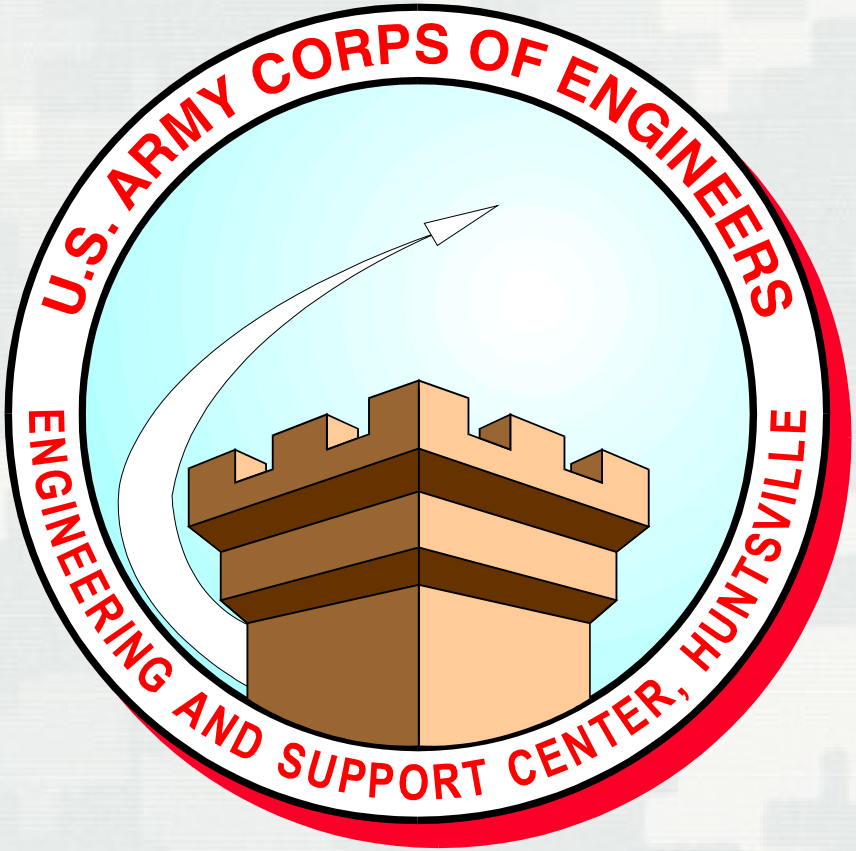
Questions?


U.S. ARMY CORPS OF ENGINEERS
ENGINEERING AND SUPPORT CENTER, HUNTSVILLE

LCS

- *Definition and Usage*
- *Control Limits and Control Charts*
- *DoD QSM V4.1 Requirements*
  - *In-House statistically-derivation*
  - *Minimum number of data points*
  - *Update frequency*
  - *Acceptance criteria*
  - *Applications*

LCS Definition and Usage

- ***EPA SW-846***
  - *LCS consists of either a control matrix spiked with analytes representative of the target analytes or a certified reference material.*
  - *Should be analyzed for each analytical method when appropriate for the method.*
  - *Should be analyzed with each batch of samples processed to verify that the precision and bias of the analytical process are within control limits.*
  - *The LCS results are compared with control limits established for both precision and bias to determine data usability.*
- ***DoD QSM V4.1***
  - *LCS: A sample matrix, free from the analytes of interest, spiked with verified known amounts of analytes or a material containing known and verified amounts of analytes.*
  - *It is generally used to establish intra-laboratory or analyst-specific precision and bias or to assess the performance of all or a portion of the measurement system.*

LCS Usage

- *LCS control limits and control charts demonstrate laboratory's performance on a clean matrix.*
- *The inability to achieve acceptable recoveries of LCS indicates problems with the precision and bias of the measurement system.*
- *Failure to achieve acceptable recoveries in a clean matrix is an indicator of possible problems achieving acceptable recoveries in field samples.*

DoD QSM V4.1 Requirements

- *Spike all target analytes, except for PCB, at project-specific concentration of concern. If not specified, spike at or below the midpoint of calibration curve.*
- *A laboratory shall establish its statistical control limits for LCS recoveries based on in-house historical data.*
- *DoD identifies poor performing analytes and allows sporadic marginal exceedances.*
- *Control charts shall be maintained and used to detect trends and prevent out of control conditions.*
- *DoD may review the laboratory in-house limits and associated trends, as reflected in control charts, to determine whether the laboratory's overall performance is acceptable. If deemed unacceptable, this can allow DoD to decide not to use the laboratory again until substantial improvement has occurred.*

Introduction to Control Chart

- *Chemical analysis involves a set of interrelated activities that convert inputs into outputs, which always contain variability.*
  - ***Chance or Common Causes**: Inherent variability exists regardless of process design or maintenance.*
  - ***Assignable or Special Causes**: Process upsets, manifested by changes in output level such as spike, shift, trend, or changes in output variability.*
- *Statistical process control (SPC) uses various statistical methodologies to improve the quality of a process by reducing the variability of outputs.*
- *A process is said to be in a state of statistical control if its outputs subjected only to Common Cause variability and possess constant mean and standard deviation.*

Introduction to Control Chart

- *Control charts, developed by Dr. Walter A. Shewhart in the 1920s, are the basic analytical tools to detect the occurrence of Special Cause variability.*
- *The presence of a Special Cause is indicated by a subgroup statistic falling outside the control limit.*
- *After eliminating Special Cause variability, process variability is reduced to its inherent variability, which may be monitored by control charts.*
- *Further reduction in process variation would require modification of the process itself.*

Control Chart Setup

- *One or more observations of an output characteristic are periodically sampled from a process at a defined frequency.*
- *A control chart is a time plot summarizing these observations using sample statistics, which is a function of the observations.*
- *Control limits are plotted on the chart based on the sampling distribution of the sample statistic being evaluated.*
- *Observations sampled at a particular time point constitute a subgroup.*
- *Subgroup statistics commonly evaluated are the average, range, standard deviation, percentage or fraction of an occurrence of an event among multiple opportunities, or the number of occurrences during a defined time period or in a defined space.*

Control Chart Usage

- *The role of control charts in SPC program:*
  - *Stage A Process Evaluation: Plot historical data on control charts to assess the current state of the process and calculate control limits for future use. Ideally ≥ 100 data points and minimum of 30 data points for single observations per subgroup.*
  - *Stage B Process Improvement: Collect process data in real time and use control charts with the calculated limits in Stage A to detect, identify, and resolve special causes.*
  - *Stage C Process Monitoring: Use control chart to monitor the process to confirm continually the state of statistical control and to react to new special causes entering the system or reoccurrence of previous special causes*

Control Chart Usage

- *Applicable to:*
  - *Variables Data: the magnitude of an output characteristic measured on a continuous numerical scale. (Most chemical data.)*
  - *Attributes Data: the frequency or count of occurrences of an event in a subgroup.*
- *Variables Data*
  - *Process Variability (Precision)*
    - *Multiple Observations per Subgroup*
      - *Subgroup Range (R chart) – MS/MSD*
      - *Subgroup Standard Deviation (s chart)*
    - *Single Observation per Subgroup*
      - *Subgroup Moving Range (MR chart) – LCS*
  - *Process Level (Bias)*
    - *Multiple Observations per Subgroup*
      - *Subgroup Average (X-Bar chart) – MS/MSD*
    - *Single Observation per Subgroup*
      - *Individual observation (I chart) – LCS*

Common Control Charts

- *Control Charts for "k" Subgroups Consisting of "i" Multiple Numerical Measurements*
  - *Monitor Process Level (Bias): X-Bar Chart*
  - *Monitor Process Variability (Precision): R Chart or s Chart*
- *Control Charts for Single Numerical Measurements*
  - *Monitor Process Level (Bias): I Chart*
  - *Monitor Process Variability (Precision): MR Chart*

Control Chart (X-Bar, R)

- *X-Bar Chart for "k" Subgroups Consisting of "i" Multiple Numerical Measurements*
  - *Mean:* $\bar{X}_i = \sum_{j=1}^{n} X_{ij} / n = (X_{i1} + X_{i2} + \ldots + X_{in}) / n$

    where X_{ij} denotes the j^{th} observation (j = 1, 2,..., n) in the i^{th} subgroup (i = 1, 2,..., k)
  - *Grand Mean:* $\bar{\bar{X}} = \sum_{i=1}^{k} \bar{X}_i / k = (\bar{X}_1 + \bar{X}_2 + \ldots + \bar{X}_k) / k$
  - *Control Limits:* $LCL = \bar{\bar{X}} - A_2 \bar{R}$

    $UCL = \bar{\bar{X}} + A_2 \bar{R}$

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Control Chart (X-Bar, R)

- *<u>R Chart</u> for "k" Subgroups Consisting of "i" <u>Multiple</u> Numerical Measurements*
  - *Range:* $R_i = Max(X_{i1}, X_{i2}, \ldots, X_{in}) - Min(X_{i1}, X_{i2}, \ldots, X_{in})$

    where $Max(X_{i1}, X_{i2}, \ldots, X_{in})$ and $Min(X_{i1}, X_{i2}, \ldots, X_{in})$ denote the maximum and minimum observations in the i^{th} subgroup (i = 1, 2,..., k), respectively.
  - *Average Range:* $\bar{R} = \sum_{i=1}^{k} R_i / k = (R_1 + R_2 + \ldots + R_k)/k$
  - *Control Limits:* $LCL = D_3\bar{R}$, $UCL = D_4\bar{R}$

Control Chart (X-Bar, s)

- *X-Bar Chart for "k" Subgroups Consisting of "i" Multiple Numerical Measurements*
  - *Mean:* $\bar{X}_i = \sum_{j=1}^{n} X_{ij} / n = (X_{i1} + X_{i2} + \ldots + X_{in}) / n$

    where X_{ij} denotes the j^{th} observation (j = 1, 2,..., n) in the i^{th} subgroup (i = 1, 2,..., k)
  - *Grand Mean:* $\bar{\bar{X}} = \sum_{i=1}^{k} \bar{X}_i / k = (\bar{X}_1 + \bar{X}_2 + \ldots + \bar{X}_k) / k$
  - *Control Limits:*

$$LCL = \bar{\bar{X}} - A_3 \bar{s}$$

$$UCL = \bar{\bar{X}} + A_3 \bar{s}$$

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Control Chart (X-Bar, s)

- *s Chart for "k" Subgroups consisting of "i" Multiple Numerical Measurements*
  - *Standard Deviation (SD):* $s_i = \sqrt{\sum_{j=1}^{n} (X_{ij} - \bar{X}_i)^2 / (n-1)}$
  - *Average SD:* $\bar{s} = \sum_{i=1}^{k} s_i / k = (s_1 + s_2 + \ldots + s_k)/k$
  - *Control Limits:* $LCL = B_3 \bar{s}$, $UCL = B_4 \bar{s}$

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Control Chart Factors

	X-Bar and R Charts			X-Bar and s Charts		
$\bar{n}$	A_2	D_3	D_4	A_3	B_3	B_4
2	1.880	0	3.264	2.659	0	3.267
3	1.023	0	2.575	1.954	0	2.568
4	0.729	0	2.282	1.628	0	2.266
5	0.577	0	2.114	1.427	0	2.089
6	0.483	0	2.004	1.287	0.030	1.970
7	0.419	0.076	1.924	1.182	0.118	1.882
8	0.373	0.136	1.864	1.099	0.185	1.815
9	0.337	0.184	1.816	1.032	0.239	1.761
10	0.308	0.223	1.777	0.975	0.284	1.716

Note: For larger "n", see ASTM E 2587

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Example Control Chart (X-Bar, s)

Vitamin tablets are compressed from blended granulated powder and tablet hardness is measured on ten tablets each hour

Subgroup	T1	T2	T3	T4	T5	T6	T7	T8	T9	T10	Mean	Std Dev
1	21.3	19.5	21.3	23.1	22.4	24.6	23.4	22.4	21.4	22.9	22.23	1.419
2	21.4	22.2	22.1	23.3	23.9	22.9	21.6	24.6	25.7	24.1	23.18	1.399
3	23.9	24.2	22.8	22.9	25.9	21.4	23.1	20.5	23.6	23.8	23.21	1.494
4	23.4	26.3	24.4	25.3	22.0	25.8	22.7	26.5	21.6	25.0	24.30	1.781
5	25.6	22.9	24.6	23.8	23.6	22.7	27.1	25.3	25.1	25.5	24.62	1.372
6	26.8	25.7	25.6	24.8	25.7	26.0	23.6	22.8	22.1	24.7	24.78	1.507
7	26.6	24.0	25.0	26.3	25.3	25.2	25.0	24.1	22.6	26.0	25.01	1.199
8	26.7	25.9	22.6	23.8	27.3	26.7	25.7	24.1	25.2	25.2	25.32	1.470
9	25.0	24.8	22.4	22.9	24.9	24.4	22.5	22.7	23.8	24.0	23.74	1.037
10	26.1	25.3	25.7	25.0	24.7	26.2	23.6	24.2	25.1	24.3	25.02	0.844
Center line											24.141	1.352
LCL											22.823	0.384
UCL											25.459	2.320
LWL											23.262	
UWL											25.020	
$L\sigma$ L											23.702	
$H\sigma$ L											24.580	

Source: ASTM Standard E 2587

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Example Control Chart (X-Bar, s)

- ***X-Bar Chart:***
  - *LCL = 24.141 – (0.975)(1.352) = 22.823*
  - *UCL = 24.141 + (0.975)(1.352) = 25.459*
  - *LWL = 24.141 – 2(0.975)(1.352)/3 = 23.262*
  - *UWL = 24.141 + 2(0.975)(1.352)/3 = 25.020*
  - *LσL = 24.141 – (0.975)(1.352)/3 = 23.702*
  - *UσL = 24.141 + (0.975)(1.352)/3 = 24.580*
- ***S Chart:***
  - *LCL = (0.284)(1.352) = 0.384*
  - *UCL = (1.716)(1.352) = 2.320*

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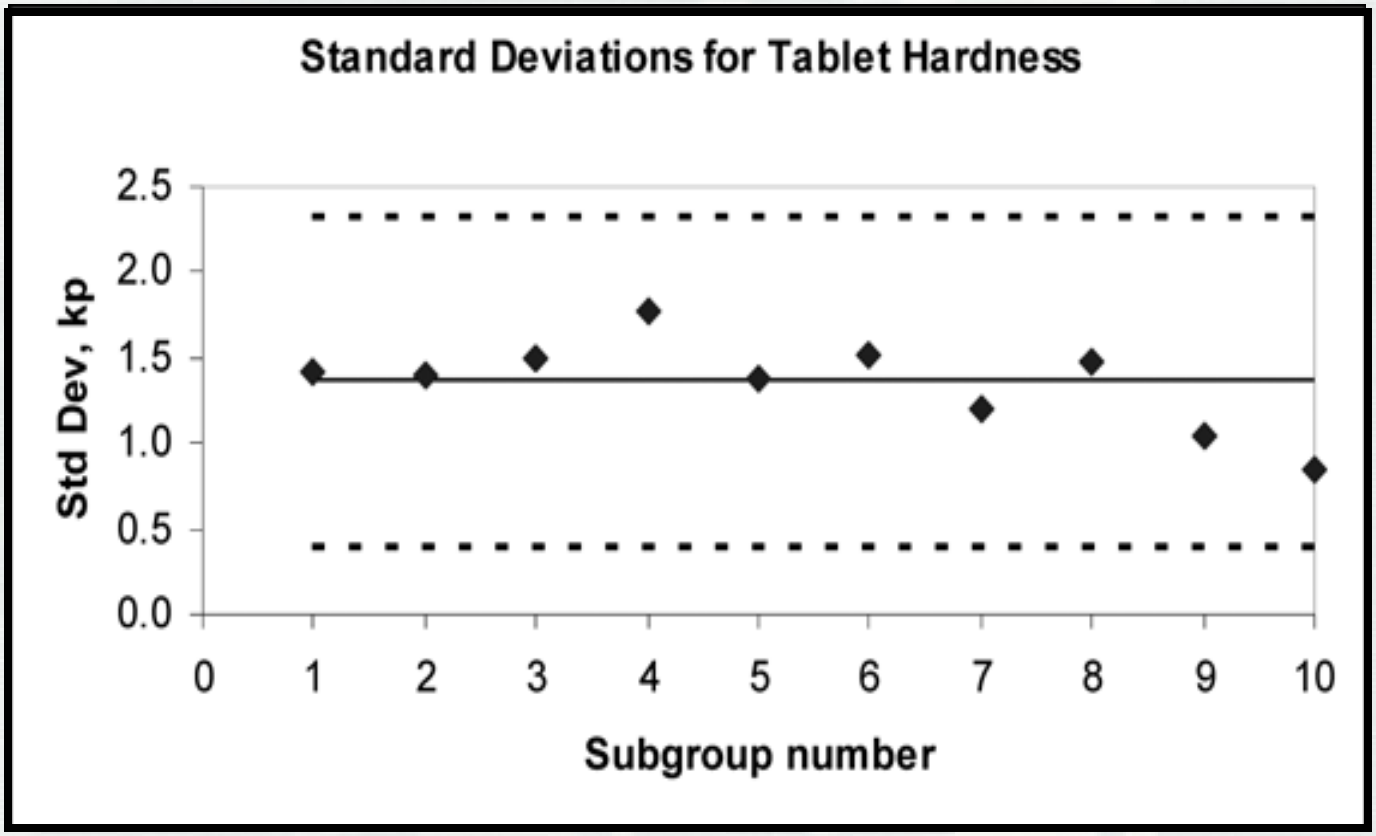
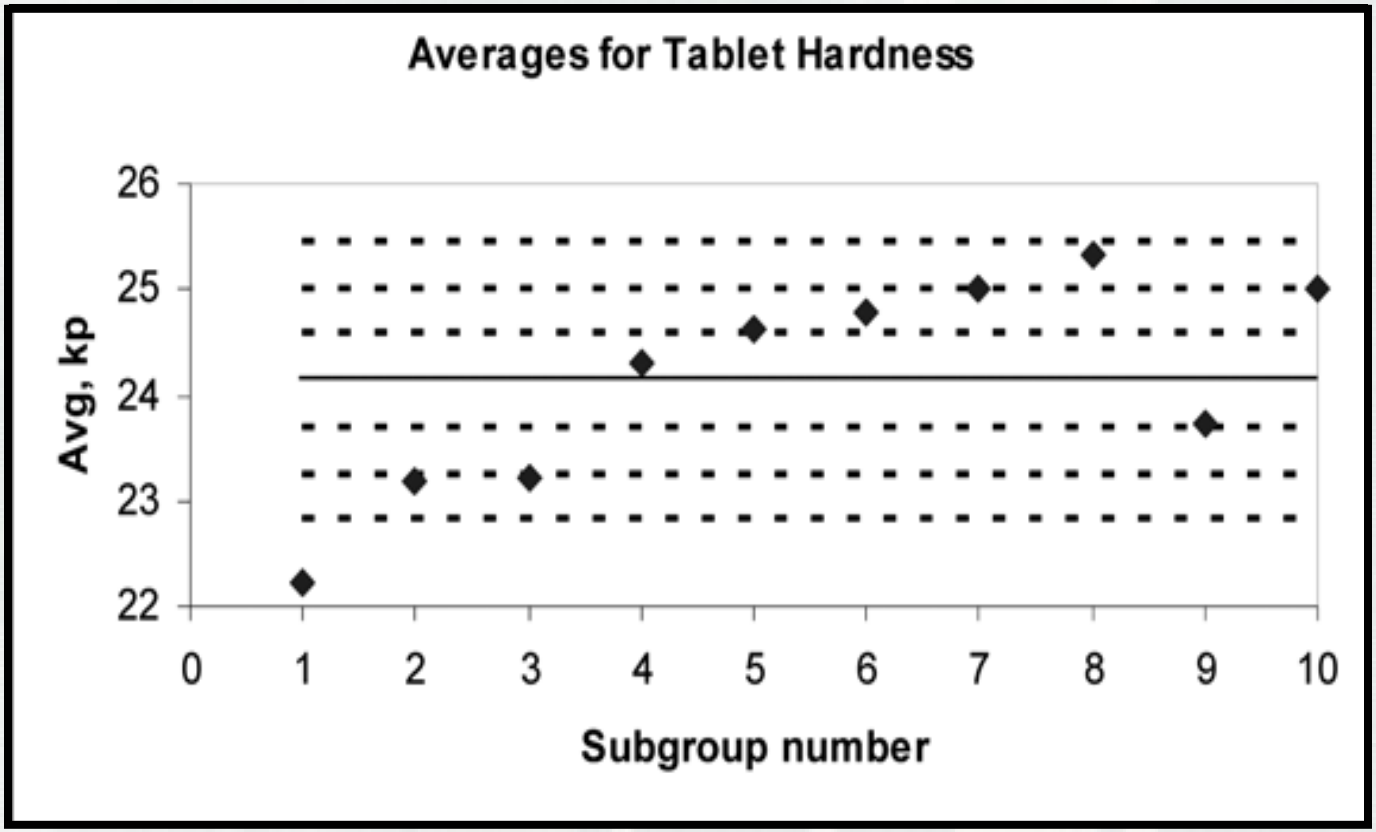
Example s Chart



Source: ASTM Standard E 2587

Example X-Bar Chart



Source: ASTM Standard E 2587

Common Control Chart Setup

- *Subgroup sampling frequency depends on:*
  - *Practical considerations, such as time and cost.*
  - *Process dynamics (how quickly the output respond to upsets).*
  - *Consequences of not reacting promptly to a process upset.*
- *Subgroup size depends on:*
  - *Normality based on Central Limit Theorem.*
  - *Practical considerations, such as time and cost.*
  - *Should be fixed for easy interpretation.*

LCS Control Chart

- *Frequency of sample analyses are usually non-regular.*
- *Frequency of LCS analysis is typically one per batch.*
- *Routine and frequent analysis of multiple LCS is often time and cost prohibitive.*
- *I chart and MR chart:*
  - *Individual observation in time order*
  - *Moving range (MR) in time order*

Control Chart (I, MR)

- *I Chart for "k" Subgroups Consisting of Single Numerical Measurement*
  - *Individual Observation:* X_i *in the* i^{th} *subgroup (i = 1, 2, …, k)*
  - *Mean:*

$$\bar{X} = \sum_{i=1}^{k} X_i / k = (X_1 + X_2 + \ldots + X_k)/k$$

  - *Control Limits:*

$$LCL = \bar{X} - 2.66\overline{MR}$$

$$UCL = \bar{X} + 2.66\overline{MR}$$

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Control Chart (I, MR)

- *MR Chart for "k - 1" Subgroups Consisting of Single Numerical Measurement*
  - *Moving Range:* $MR_i = |X_i - X_{i-1}|$

    where MR_i is the absolute value of the difference between two successive values for k – 1 subgroups, i = 2, 3,..., k.
  - *Average Moving Range:*

$$\overline{MR} = \sum_{i=2}^{k} MR_i/(k-1) = (MR_2 + MR_3 + \ldots + MR_k)/(k-1)$$

  - *Control Limits:*

$$LCL = 0$$

$$UCL = 3.27\overline{MR}$$

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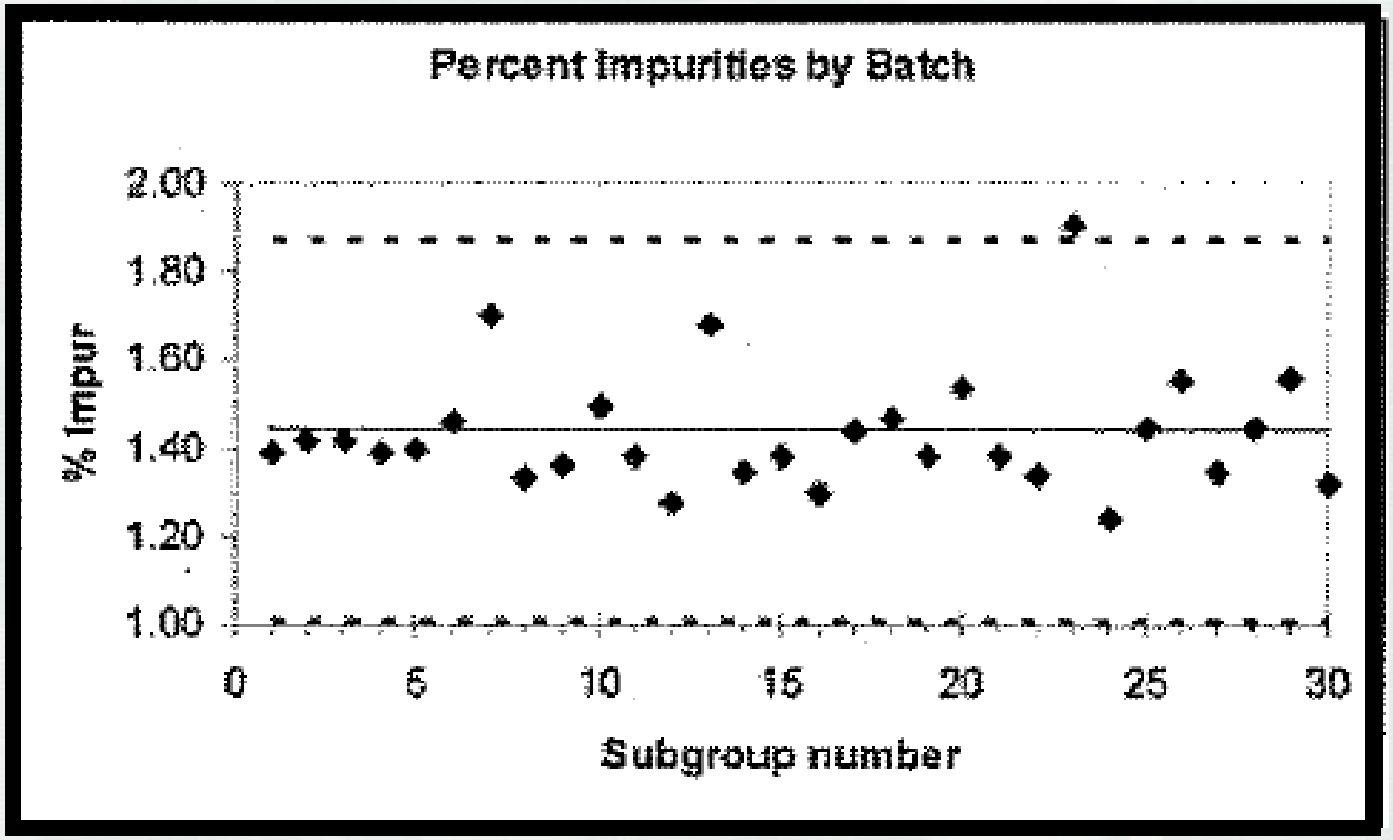
Example Control Chart (I, MR)

30 batches of polymers are sampled and analyzed for an impurity reported as weight percent

Subgroup	Impurity	MR	Subgroup	Impurity	MR	Subgroup	Impurity	MR
1	1.39	---	11	1.38	0.12	21	1.38	0.16
2	1.42	0.03	12	1.28	0.10	22	1.34	0.04
3	1.42	0.00	13	1.68	0.40	23	1.91	0.57
4	1.39	0.03	14	1.35	0.33	24	1.24	0.67
5	1.40	0.01	15	1.38	0.03	25	1.45	0.21
6	1.46	0.06	16	1.30	0.08	26	1.55	0.10
7	1.70	0.24	17	1.44	0.14	27	1.35	0.20
8	1.33	0.37	18	1.47	0.03	28	1.45	0.10
9	1.36	0.03	19	1.38	0.09	29	1.56	0.11
10	1.50	0.14	20	1.54	0.16	30	1.32	0.24
						Mean	1.437	0.165
						LCL	0.998	0
						UCL	1.877	0.540

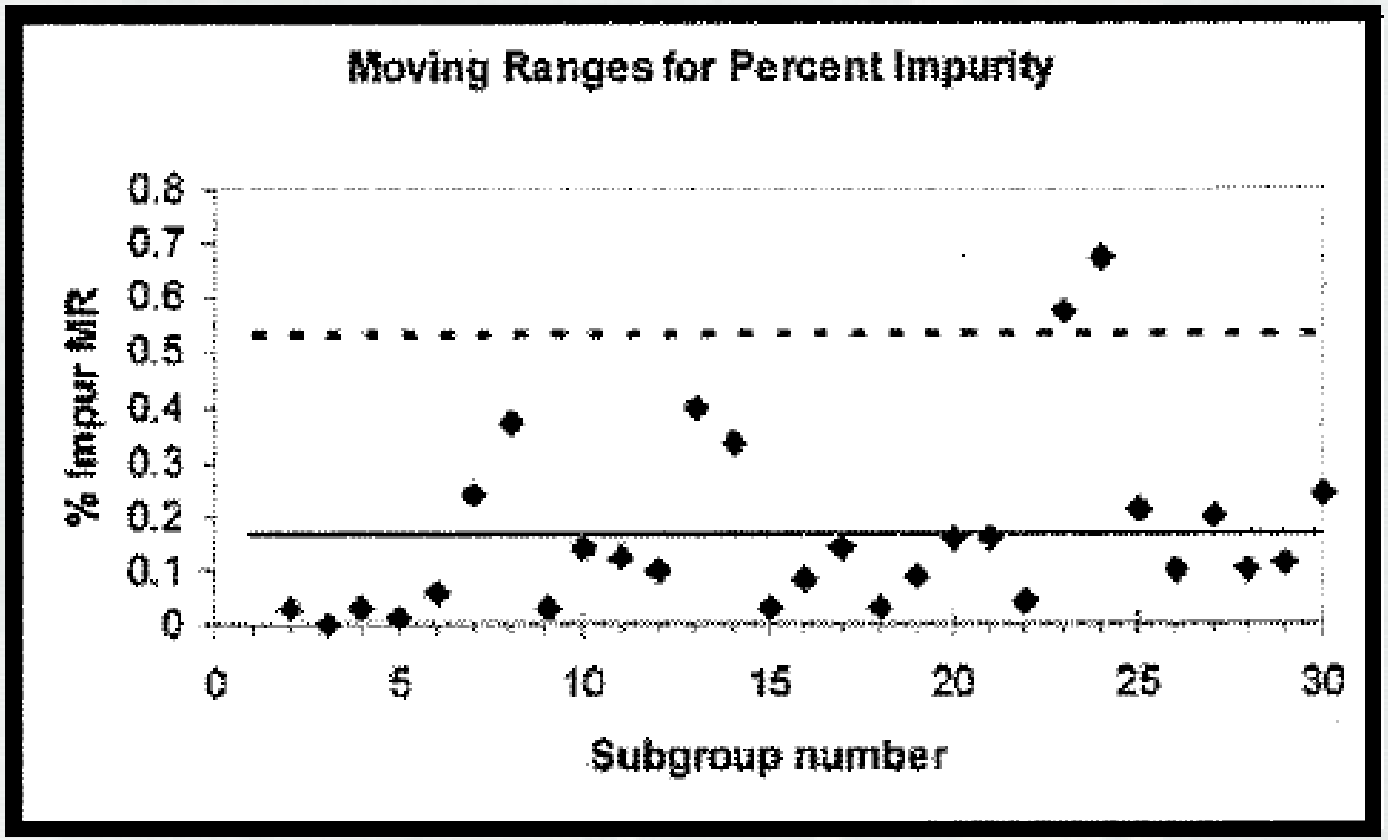
Source: ASTM Standard E 2587

Example I Chart



Source: ASTM Standard E 2587

Example MR Chart



Source: ASTM Standard E 2587

I and MR Charts for LCS

- *Used for subgroups consisting of a single numerical measurements.*
- *I chart monitors process level and MR chart monitors variable-term variability, compared with short-term variability of R chart.*
- *Some practitioners state that MR chart does not add value and recommend against its use for other than calculating the control limits for the I chart.*
- *I and MR charts of single observations are not equivalent to X-Bar and R charts of multiple observations.*

DoD QSM V4.1 Requirements

Positive and Negative Controls: LCS Control Limits (Requirement)

A laboratory shall establish in-house limits that:

- Are statistically-derived using scientifically valid and documented procedures;
- Meet the limits specified by the project or as stated in the method, if available;
- Are updated on an annual basis, or as stated in the method, and re-established after major changes in the analytical process (e.g., new instrumentation);
- Are based on at least 30 data points generated under the same analytical process;
- Do not exclude failed LCS recovery data and statistical outliers from the calculation, unless there is a documented and scientifically valid reason (e.g., bad LCS standard, leaking purging cell);

Control limits may not be greater than ± 3 times the standard deviation of the mean LCS recovery. Control charts shall be maintained and used to detect trends and prevent out-of-control conditions. Control limits shall be continually monitored for shifts in mean recovery, changes in standard deviation, and development of trends.

D-3

DoD QSM V4.1 Requirements

- *DoD QSM V4.1 requires a laboratory establish in-house statistically-derived control limits using scientifically valid and documented procedures.*
  - *EPA OSW SW-846, Chapter ONE, Section 4.4.2:*

    "Typically, control limits for bias are based on the historical mean recovery plus or minus three standard deviation units, and control limits for precision range from zero (no difference between duplicate control samples) to the historical mean relative percent difference plus three standard deviation units."
  - *EPA OW EPA-600/4-79-019, "Handbook for Analytical Quality Control in Water and Wastewater Laboratories".*
  - *Standard Methods for Examination of Water and Wastewater, 1020 B "Quality Control".*
  - *ASTM E 2587, "Use of Control Charts in Statistical Process Control".*

DoD QSM V4.1 Requirements

Positive and Negative Controls: LCS Spiking Compounds (Requirement)

- All target analytes must be spiked in the LCS (with the exception of PCB analysis, which is spiked per the method). Target analytes are identified by the client on a project-specific basis. This may require the preparation of multiple LCSs to avoid interferences.
- The concentration of the spiked compounds shall be at the project-specific concentration of concern. If this is not specified, it shall be at or below the midpoint of the calibration curve.

D-2

Positive and Negative Controls: LCS Marginal Exceedance (ME) Limits (Requirement)

The marginal exceedance limit is four (4) standard deviations around the mean.

D-4

Positive and Negative Controls: Target Analytes (Requirement)

DoD does not allow any target analyte to exceed its LCS control limits, even marginally. It is inappropriate to control batch acceptance on poor-performing analytes.

D-5

Positive and Negative Controls: Random Marginal Exceedance (Clarification)

DoD considers the same analyte exceeding the LCS control limit two (2) out of three (3) consecutive LCS to be indicative of non-random behavior.

D-6

DoD QSM V4.1 Requirement Summary

- *A laboratory must establish, use, and maintain control charts for the LCS. (Box D-3)*
- *A laboratory shall establish statistically-based LCS control limits based on ≥ 30 in-house historical data points, using scientifically valid and documented procedures. (Box D-3)*
- *LCS control limits shall be ≤ mean ± 3s. (Box D-3)*
- *Update annually or as stated in the method, and re-establish after major changes in the method process. (Box D-3)*
- *Do not exclude failed LCS or outliers, unless there is documented and scientifically valid reason. (Box D-3)*
- *Acknowledge poor performing analytes, which do not control batch acceptance. (Box D-5 & Table G-2)*
- *Meet the project-specific requirements. (Box D-3)*
- *Allows a limited number of sporadic marginal exceedances of ± 4s (Boxes D-4 & D-6, Table G-1)*
- *No exceedance is allowed for any project-specific target analyte. (Box D-5)*

Control Chart Suggestions

- *Annually establish LCS control limits based on the mean ± 3s of ≥ 30 most recent LCS recovery data points.*
- *After each 15 new LCS recovery measurements, a laboratory may calculate its control limits using the most recent 30 data points and statistically compared the calculated limits with the previously established control limits to determine if the previously established control limits are still acceptable or need update.*
- *If it is determined that previously determined control limits are still acceptable, the laboratory may continually use previous control limits; otherwise, establish new control limits based on new data.*
- *Statistical tests such as Student's t test and F test may be used to test the existence of variations in mean and variance. Test of data distribution for normality is recommended prior to t and F tests.*
- *If the means and variances of two data sets are not statistically different and there were no changes in laboratory operations, a laboratory may pool all data to determine the mean and standard deviation.*

DoD QSM V4.1 Approach Marginal Exceedance

- *Based on binomial distribution of random variables that meet **BINS** conditions of **B**inary outcomes, **I**ndependent trials with fixed **N**umber of trials and the **S**ame probability for all trials.*
- *Determine the maximum allowable number of target analytes that will sporadically fall outside ±3s control limits at 99% confidence.*
- *For example, if there are 65 target analytes for an LCS analysis of semivolatile organics by Method 8270C, how many target analytes could fail their ± 3s control limits at 99% confidence because of random errors?*

DoD QSM V4.1 Approach Marginal Exceedance

- *Using a coin-flip analogy, there is a 50% probability for each coin to show head; however, there is a less than 50% probability for all 65 coins to show heads. The probability for all 65 coins to show heads is $(0.5)^{65}$ or 2.71×10^{-18}%.*
- *Similarly, there is about a 99% probability for each of 65 target analytes falling into its ± 3s control limits; however, there is a less than 99% probability for all 65 target analytes fall into their individual ± 3s control limits. The probability to have all 65 target analytes fall into their ± 3s control limits would be $(0.99)^{65}$ or 52.03%, which means there is a 47.97% probability that a laboratory may have one or more target analytes fall outside ± 3s control limits because of random error.*
- *The probability of 47.97% random error failures is very high and a laboratory could always claim that its LCS failure (i.e., not all target analytes passed) is probably due to random errors, instead of laboratory performance problems.*

DoD QSM V4.1 Approach Marginal Exceedance

- *Therefore, DoD allows certain number of target analytes outside their individual ± 3s control limits so that a laboratory cannot reasonably blame random errors but accepts the fact that the laboratory most likely (i.e., 99%) has performance problems.*
- *Based on binomial distribution, the cumulative probability is equal to:*

$$Pr\{\leq j \text{ outside } \pm 3s\} = \sum {}_nC_j \, p^j \, (1 - p)^{n-j}$$

where the summation runs from 0 to j and ${}_nC_j$ is a binomial coefficient and p is the probability (i.e., 1%) that a target analyte will fall outside the control limits of the mean ± 3s.

DoD QSM V4.1 Approach Marginal Exceedance

- *For example, the probability for up to 3 target analytes out of a total of 65 target analytes of Method 8270C falling outside their individual "mean ± 3s" control limits will be:*

$$Pr\{\leq 3 \text{ outside } \pm 3s\} = {}_{65}C_0\,(0.01)^0\,(1-0.01)^{65-0} + {}_{65}C_1\,(0.01)^1\,(1-0.01)^{65-1} + {}_{65}C_2\,(0.01)^2\,(1-0.01)^{65-2} + {}_{65}C_3\,(0.01)^3\,(1-0.01)^{65-3} = 99.58\%$$

- *There is a very low probability of 0.42% that more than 3 target analytes will simultaneously fall outside their individual "mean ± 3s" control limits. If a laboratory has more than three LCS target analytes outside their "mean ± 3s" control limits, the failure is probably (i.e., 99.58%) due to poor laboratory performance, instead of random errors.*

DoD QSM V4.1 Approach Marginal Exceedance

- ***M**aximum **A**llowable **N**umber of **S**poradic **F**ailures (**MANSF**): based on cumulative probability for j number of targets out of a total n number of target analytes fall outside ± 3s control limits at 99% confidence.*

n (# of target analytes)	***j (MANSF)***
2 – 19	***1***
20 – 52	***2***
53 – 95	***3***

- *DoD QSM* **Table G-1. Number of Marginal Exceedances** *umber of LCS analytes.*

Number of Analytes in LCS	Allowable Number of Marginal Exceedances of LCS-CLs
> 90	5
71 – 90	4
51 – 70	3
31 – 50	2
11 – 30	1
< 11	0

DoD QSM V4.1 Policy on LCS Evaluation

DoD LCS Control Limits Policy

- The laboratory shall use project-specific control limits based on data quality objectives (DQOs), if available. If not, DoD-generated LCS-CLs shall be used, if available. Otherwise, the laboratory's own in-house control limits shall be used.
- The LCS-CLs are based on the promulgated versions of SW-846 methods at the time of the study (2000). They should be used as a benchmark to evaluate acceptability even as methods are updated or alternative methods for the same class of compounds become available.
- The fact that the LCS-CLs are based on certain SW-846 methods should not limit the use of alternative analytical methods, if appropriate. If an alternative method is used, however, it should be capable of producing LCS recoveries that are at least as good as the DoD-generated LCS-CLs, unless project-specific DQOs allow less stringent criteria.
- The LCS study shows that preparatory methods may have a significant influence on a laboratory's ability to achieve certain LCS-CLs. If a laboratory is unable to achieve the LCS-CLs presented in this appendix, it should investigate the use of alternative preparatory methods as a means to improve precision and accuracy.

Source: DoD QSM V4.1 Appendix G

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DoD QSM V4.1 Approach

- *In-house LCS control limits and control charts are used for:*
  - *Demonstration of laboratory performance*
  - *Batch quality control*
  - *Trend analysis and performance monitoring and improvement*
- *A laboratory with in-house LCS control limits outside project-specified LCS acceptance limits are considered not qualified for DoD sample analysis, until it improves its in-house limits.*
  - *The project may select a different laboratory, method, or relax the data quality requirements.*

DoD QSM V4.1 Approach

- *The acceptability of LCS results shall be based on project-specified limits or defaulted to the DoD QSM LCS control limits (Appendix G) if project-specified limits are not available. If DoD QSM limits are not available either, the laboratory must use its in-house limits for batch acceptance.*
- *A laboratory shall establish and maintain its own in-house LCS limits, which must be consistent with (i.e., within) the DoD limits that are project-specific limit, if available; otherwise, the DoD QSM limits.*
- *A laboratory's in-house limits shall be calculated from its historical LCS data in accordance with a documented procedure that is consistent with good laboratory practice.*

DoD QSM V4.1 Approach

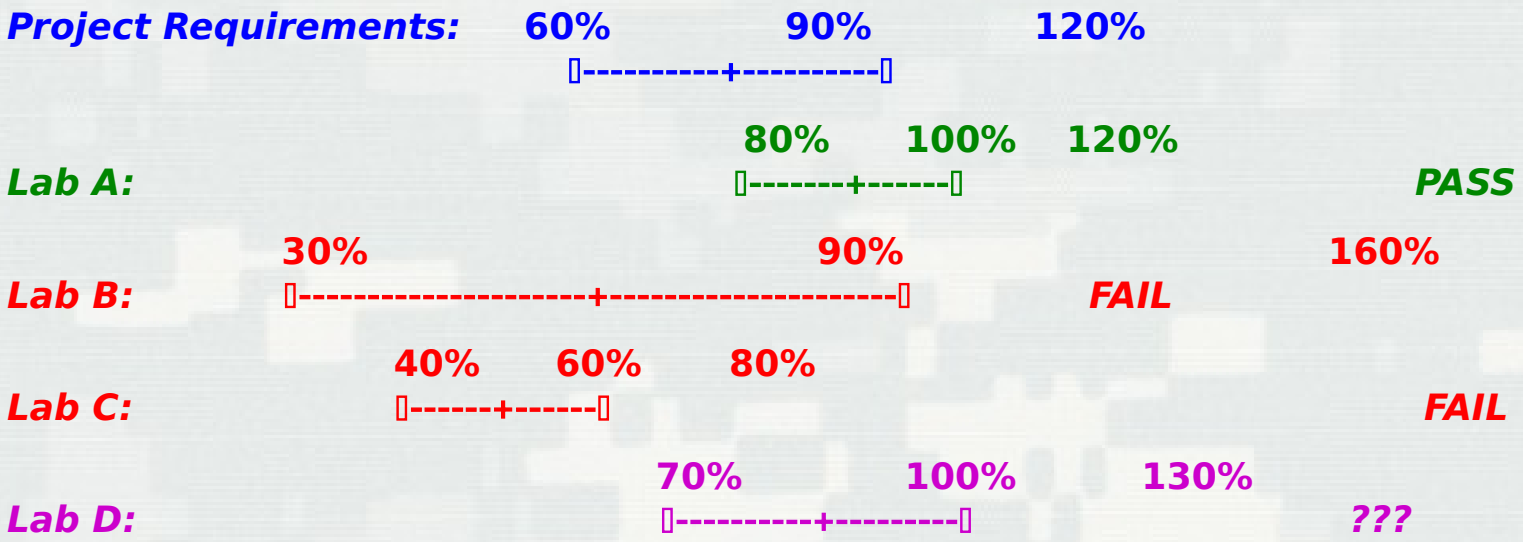
- *If a laboratory's in-house limits are outside the DoD control limits (upper and/or lower), the laboratory must report its in-house limits in the laboratory report (see Appendix E) even if the LCS associated with the batch fell within the DoD limits.*
  - *This information allows DoD to determine the data quality and usability.*
- *DoD will review a laboratory in-house limits and associated trends, as reflected in control charts, to determine whether the laboratory's overall performance is acceptable. If deemed unacceptable, DoD may stop sample analysis or not use the laboratory again until substantial improvement has occurred.*

DoD QSM V4.1 Approach

- *If a laboratory's in-house control limits are consistent with (i.e., within) the project-specified acceptance limits, the laboratory shall use its in-house control limits in the following manners:*
  - *The laboratory should use its tighter in-house limits to monitor laboratory performance.*
  - *The laboratory is allow to report samples results with LCS recoveries that fall outside of its in-house limits but within project-specified acceptance limits.*
  - *The laboratory should investigate the out-of-control event and take appropriate corrective actions to bring the analytical system back into control.*

DoD QSM V4.1 Approach

- *Following examples demonstrate different situations between laboratory in-house control limits and Project requirements.*



- *Does **Lab D** pass?*

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Proposed DoD QSM Approach

Critical Values of Student's *t* Distribution

df	Upper Tail Probability 0.20	0.10	0.05	0.04	0.03	0.025	0.02	0.01	0.005	0.0005
1	1.376	3.078	6.314	7.916	10.579	12.706	15.895	31.821	63.657	636.619
2	1.061	1.886	2.920	3.320	3.896	4.303	4.849	6.965	9.925	31.599
3	0.978	1.638	2.353	2.605	2.951	3.182	3.482	4.541	5.841	12.924
4	0.941	1.533	2.132	2.333	2.601	2.776	2.999	3.747	4.604	8.610
5	0.920	1.476	2.015	2.191	2.422	2.571	2.757	3.365	4.032	6.869
6	0.906	1.440	1.943	2.104	2.313	2.447	2.612	3.143	3.707	5.959
7	0.896	1.415	1.895	2.046	2.241	2.365	2.517	2.998	3.499	5.408
8	0.889	1.397	1.860	2.004	2.189	2.306	2.449	2.896	3.355	5.041
9	0.883	1.383	1.833	1.973	2.150	2.262	2.398	2.821	3.250	4.781
10	0.879	1.372	1.812	1.948	2.120	2.228	2.359	2.764	3.169	4.587
11	0.876	1.363	1.796	1.928	2.096	2.201	2.328	2.718	3.106	4.437
12	0.873	1.356	1.782	1.912	2.076	2.179	2.303	2.681	3.055	4.318
13	0.870	1.350	1.771	1.899	2.060	2.160	2.282	2.650	3.012	4.221
14	0.868	1.345	1.761	1.888	2.046	2.145	2.264	2.624	2.977	4.140
15	0.866	1.341	1.753	1.878	2.034	2.131	2.249	2.602	2.947	4.073
16	0.865	1.337	1.746	1.869	2.024	2.120	2.235	2.583	2.921	4.015
17	0.863	1.333	1.740	1.862	2.015	2.110	2.224	2.567	2.898	3.965
18	0.862	1.330	1.734	1.855	2.007	2.101	2.214	2.552	2.878	3.922
19	0.861	1.328	1.729	1.850	2.000	2.093	2.205	2.539	2.861	3.883
20	0.860	1.325	1.725	1.844	1.994	2.086	2.197	2.528	2.845	3.850
21	0.859	1.323	1.721	1.840	1.988	2.080	2.189	2.518	2.831	3.819
22	0.858	1.321	1.717	1.835	1.983	2.074	2.183	2.508	2.819	3.792
23	0.858	1.319	1.714	1.832	1.978	2.069	2.177	2.500	2.807	3.768
24	0.857	1.318	1.711	1.828	1.974	2.064	2.172	2.492	2.797	3.745
25	0.856	1.316	1.708	1.825	1.970	2.060	2.167	2.485	2.787	3.725
26	0.856	1.315	1.706	1.822	1.967	2.056	2.162	2.479	2.779	3.707
27	0.855	1.314	1.703	1.819	1.963	2.052	2.158	2.473	2.771	3.690
28	0.855	1.313	1.701	1.817	1.960	2.048	2.154	2.467	2.763	3.674
29	0.854	1.311	1.699	1.814	1.957	2.045	2.150	2.462	2.756	3.659
30	0.854	1.310	1.697	1.812	1.955	2.042	2.147	2.457	2.750	3.646
40	0.851	1.303	1.684	1.796	1.936	2.021	2.123	2.423	2.704	3.551
50	0.849	1.299	1.676	1.787	1.924	2.009	2.109	2.403	2.678	3.496
60	0.848	1.296	1.671	1.781	1.917	2.000	2.099	2.390	2.660	3.460
70	0.847	1.294	1.667	1.776	1.912	1.994	2.093	2.381	2.648	3.435
80	0.846	1.292	1.664	1.773	1.908	1.990	2.088	2.374	2.639	3.416
100	0.845	1.290	1.660	1.769	1.902	1.984	2.081	2.364	2.626	3.390
140	0.844	1.288	1.656	1.763	1.896	1.977	2.073	2.353	2.611	3.361
1000	0.842	1.282	1.646	1.752	1.883	1.962	2.056	2.330	2.581	3.300
∞	0.842	1.282	1.645	1.751	1.881	1.960	2.054	2.326	2.576	3.291
	60%	80%	90%	92%	94%	95%	96%	98%	99%	99.9%

Confidence Level

Two-tail Student's t value for 99% confidence level with n-1 degrees of freedom (n = 30), $t_{(n-1,\ 1-\alpha=0.99)}$ **= 2.756.**

2.756

3 ÷ 2.756 = 109%

2.756 ÷ 3 = 0.92

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Proposed DoD QSM Approach

- *Due to small sample size (n = 30), LCS control limits that are slightly outside the project-specified acceptance limits may be acceptable, if either of the following condition met:*
  - *Student's t adjusted LCS control limits are within project-specified acceptance limits.*

$$Adjusted\ UCL = UCL \times \frac{t_{(n-1,1-\alpha=0.99)}}{3} = UCL \times \frac{2.756}{3} = UCL \times 0.92$$

$$Adjusted\ LCL = LCL \div \frac{t_{(n-1,1-\alpha=0.99)}}{3} = UCL \div \frac{2.756}{3} = LCL \div 0.92$$

Lab D: *Adjusted UCL = 130% × 0.92 = 119.6% < 120%* **PASS**

  - *The laboratory's warning limits (i.e., mean ± 2s) are within project-specified acceptance limits if the objectives for completeness do not exceed 95%.*

Lab D: *LCS CL = 70 – 130% ⇒ LCS WL = 80 – 120%* **PASS**

- *Need client and regulator approval prior to use.*

Proposed DoD QSM Approach

- *The proposed approaches may not be applicable to project-specified acceptance limits that are based on the DoD QSM LCS control limits because:*
  - *DoD QSM limits were based on multiple laboratory data. Single laboratory control limits should be tighter than multiple laboratory limits.*
  - *DoD QSM limits were based on 10 year old data.*
  - *Certain DoD QSM limits and criteria were already adjusted.*

QSM V3:

SW-846 METHOD 8270 SOLID MATRIX[15]

Analyte	Mean	Standard Deviation	Lower Control Limit	Upper Control Limit	Lower ME Limit	Upper ME Limit
1,2-Dichlorobenzene	70.9	8.7	45	95	35	105

QSM V4.1:

Table G-7. LCS Control Limits for Semivolatile Organic Compounds
SW-846 Method 8270 Solid Matrix[6] (continued)

Analyte	Mean	Standard Deviation	Lower Control Limit	Upper Control Limit	Lower ME Limit	Upper ME Limit
1,2-Dichlorobenzene	70.9	8.7	45	100	35	105

DoD QSM V4.1 Approach

- *Update of LCS control limits to reflect laboratory's true and current performance.*
- *Frequency of evaluation and/or updates depends on:*
  - *At least annually*
  - *Changes in analytical operations*
  - *Changes in laboratory performance*
  - *Frequency and number of LCS analysis*

DoD QSM V4.1 Approach

- *A laboratory should test data distribution (i.e., normality) and screen outliers prior to use of proper statistic tests.*
- *Statistical outliers should not be removed from evaluation of control charts unless there is scientific evidence for removal; otherwise, the in-house control limits may be inappropriately tightened and lead to higher LCS failure rate in the future.*
- *If data are not normal distribution, then the control limits will not necessarily be representative of actual method performance.*
- *It is recommended that procedures in EPA guidance documents QA/G-9R and QA/G-9S be used for establishing statistically-derived LCS control limits.*

DoD QSM V4.1 Approach

- *Control chart must indicate the conditions under which it was developed and, at a minimum, include the following information:*
  - *Laboratory name*
  - *Analyte*
  - *Matrix*
  - *Preparation methods*
  - *Analytical method*
  - *Chart title, e.g., "Mean" or "Range" control chart.*
  - *Spike concentration*
  - *Mean, standard deviation, UCL, LCL, UWL, LWL, and the number of points.*
  - *Beginning and ending dates of LCS data collection periods.*

Suggested Trend Analysis

- ***Presence of Special Cause variation may be indicated by certain nonrandom patterns detected by the Western Electric Rules.***
  1. ***One value falls outside either control limits (± 3s) [spike].***
  2. ***Two out of three consecutive values fall outside the warning limits (± 2s) on the same side [shift].***
  3. ***Four out of five consecutive values fall outside the ± 1s limits on the same side [shift].***
  4. ***Eight consecutive values either fall above or fall below the center line [shift].***
  5. ***Six consecutive values in a row are steadily increasing or decreasing [trend].***
  6. ***Fifteen consecutive values are all within the ± 1s limits on either side of the center line [trend].***
  7. ***Fourteen consecutive values are alternating up and down [trend].***
  8. ***Eight consecutive values are outsides the ± 1s limits [trend].***
- ***Use these rules judiciously due to risk of a false alarm.***
- ***Other out-of-control Indicators:***
  1. ***< 50% initializing data fall within the ± 1s limits.***
  2. ***Measurements never or rarely outside the warning limits.***

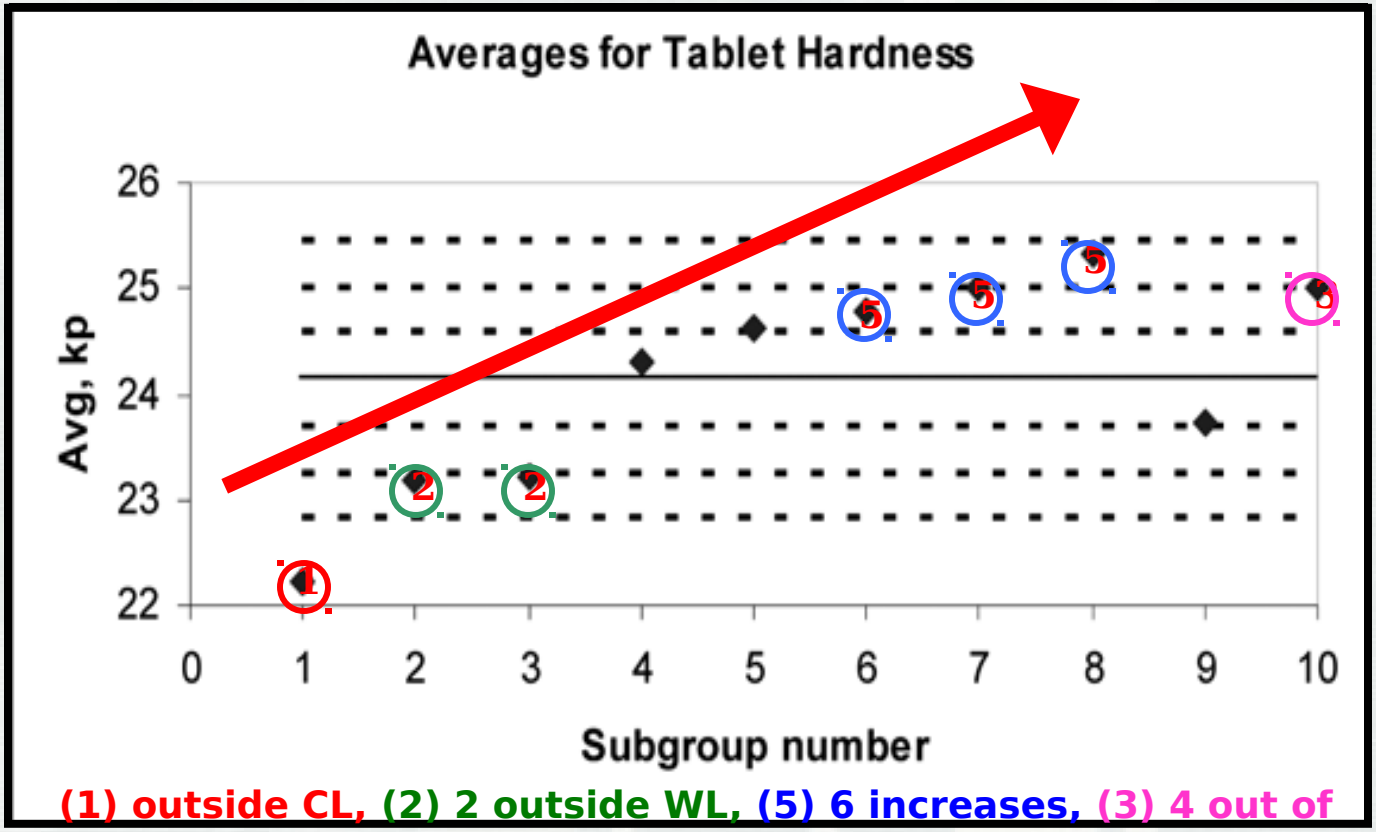
Example Trend Analysis

Vitamin tablets are compressed from blended granulated powder and tablet hardness is measured on ten tablets each hour

Subgroup	T1	T2	T3	T4	T5	T6	T7	T8	T9	T10	Mean	Std Dev
1	21.3	19.5	21.3	23.1	22.4	24.6	23.4	22.4	21.4	22.9	22.23	1.419
2	21.4	22.2	22.1	23.3	23.9	22.9	21.6	24.6	25.7	24.1	23.18	1.399
3	23.9	24.2	22.8	22.9	25.9	21.4	23.1	20.5	23.6	23.8	23.21	1.494
4	23.4	26.3	24.4	25.3	22.0	25.8	22.7	26.5	21.6	25.0	24.30	1.781
5	25.6	22.9	24.6	23.8	23.6	22.7	27.1	25.3	25.1	25.5	24.62	1.372
6	26.8	25.7	25.6	24.8	25.7	26.0	23.6	22.8	22.1	24.7	24.78	1.507
7	26.6	24.0	25.0	26.3	25.3	25.2	25.0	24.1	22.6	26.0	25.01	1.199
8	26.7	25.9	22.6	23.8	27.3	26.7	25.7	24.1	25.2	25.2	25.32	1.470
9	25.0	24.8	22.4	22.9	24.9	24.4	22.5	22.7	23.8	24.0	23.74	1.037
10	26.1	25.3	25.7	25.0	24.7	26.2	23.6	24.2	25.1	24.3	25.02	0.844
Center line											24.141	1.352
LCL											22.823	0.384
UCL											25.459	2.320
LWL											23.262	
UWL											25.020	
LσL											23.702	
HσL											24.580	

Source: ASTM Standard E 2587

Example Trend Analysis



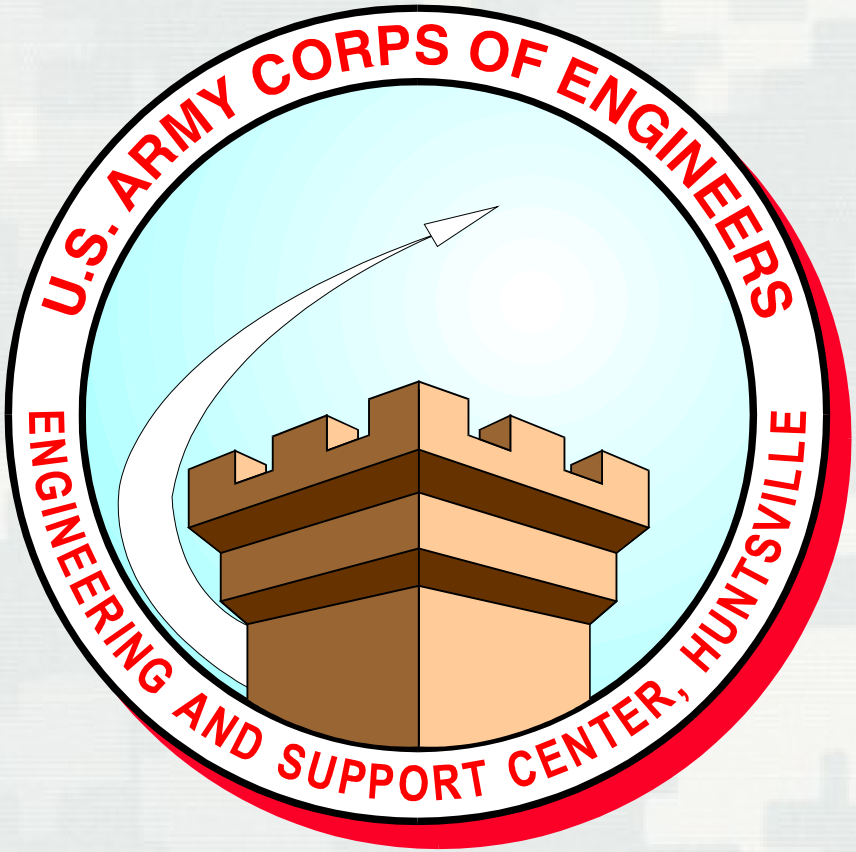
(1) outside CL, (2) 2 outside WL, (5) 6 increases, (3) 4 out of 5 outside 1s.

Source: ASTM Standard E 2587

Common Deficiencies

- Use client, contract, or method control limits for batch control when in-house limits fail.
  - ► Laboratory performance and data quality are not reflected by LCS control limits.
  - ► EPA may treat it as a laboratory fraud.
  - ► Laboratories needs to improve in-house performance, use alternative methods or in-house control limits.

Questions?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Project Applications

- *Introduction – Overview*
- *Procedures for establishing project-specific Measurement Quality Objectives (MQOs)*
- *Select analytical chemistry laboratories*
- *Case study*
- *Issues and summary*

Introduction

- *Data quality plays an important role in decision making but is often not adequately addressed in project planning or for decision making.*
- *Present a simple procedure for establishing the minimum project-specific MQOs on Data Quality Indicators (DQIs) precision, bias, and sensitivity based on project Data Quality Objectives (DQOs).*
- *Perform "Project-Specific Review" to select the appropriate DoD ELAP accredited laboratory based on the project-specific DQIs.*

Overview of DQIs

- ***Precision***: *Variability; measured by relative percent difference (RPD) of duplicates or standard deviation of LCS recoveries.*
- ***Bias***: *Difference between measured and true values; measured by percent recoveries (%Rs) of spikes or mean percent recovery of LCS.*
- ***Sensitivity***: *Smallest level for reliably reporting analyte concentrations; measured by the LOD and LOQ.*

How Are MQOs Commonly Established?

- *Copy MQOs from other projects*
- *Use method performance data*
- *Use laboratory performance data*
- *Follow program or regulatory requirements*
- *EPA QA-G/4 DQO process ???*

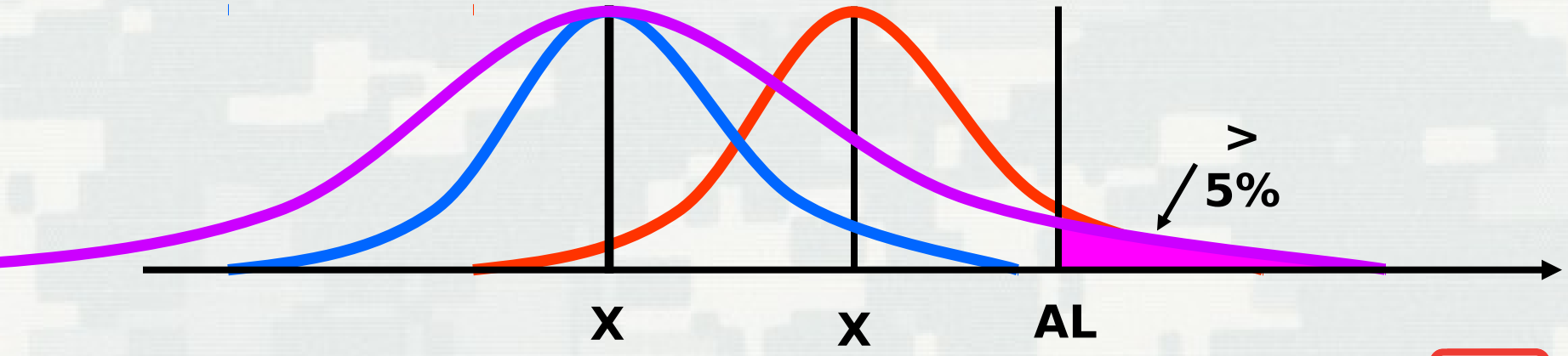
Common Reasons for Lacking Project-Specific MQOs

- *Don't know how*
- *Unknown data uncertainty prior to analysis*
- *Huge field sampling errors*
- *Limited resources*
- *No simple, reliable, and cost-effective method*
- *???*

Data Quality & Decision Error

Is [X] < AL?

Is [X] < AL @ 95% confidence?

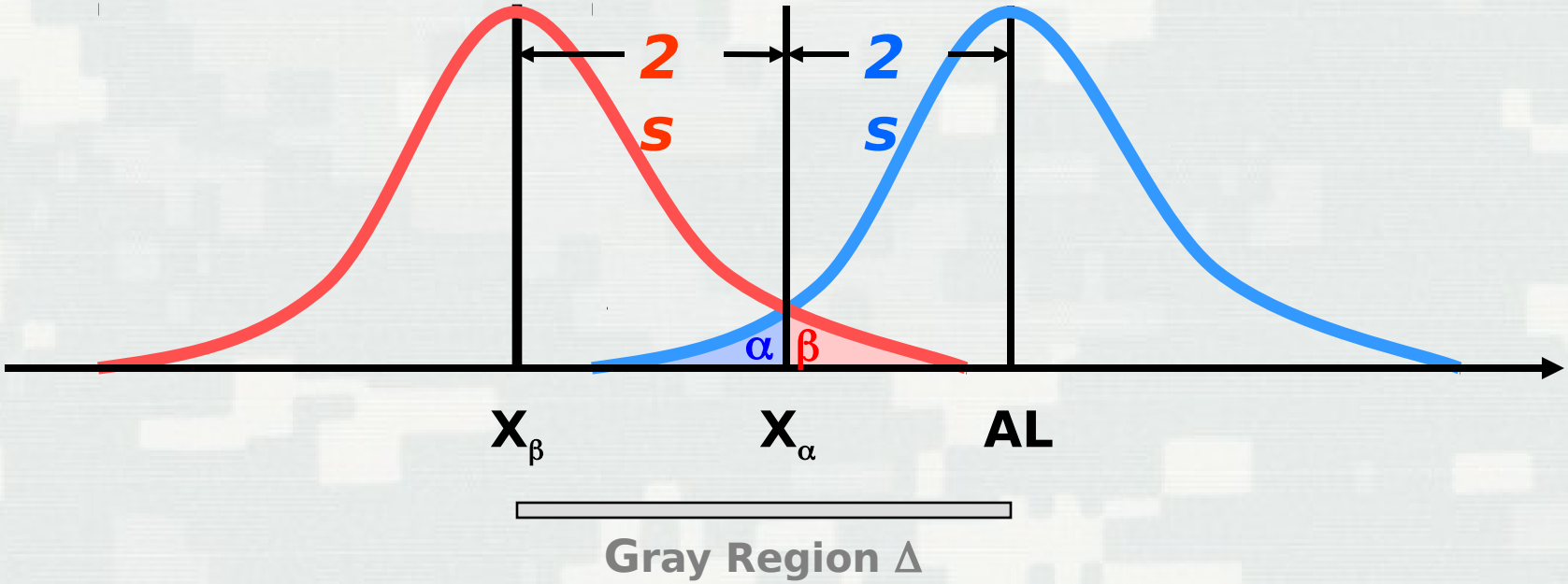


Inputs for Establishing MQOs

- *Minimum project-specific MQOs may be established based on:*
  - *Action level (AL): Regulatory level, background, risk-based level, etc.*
  - *Expected data quality: Based on DQOs, method, publication, etc.*
  - *Tolerable decision errors: α , β*

Data Quality & Decision Error

H_0: X > AL, H_A: X ≤ AL; decision errors $\alpha = \beta = 0.05$



$X_\beta = AL - \Delta = AL - 4s$, *where s = standard deviation.*

If $X \leq X_\alpha$, *site clean; if* $X \leq X_\beta$, $\alpha = \beta \leq 0.05$

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Definition of RL & LOQ

- ***RL**: Client-specified lowest concentration that meets project requirements for quantitative data with known precision and bias for a specific analyte in a specific matrix.*

  – ***DoD QSM V4.1***

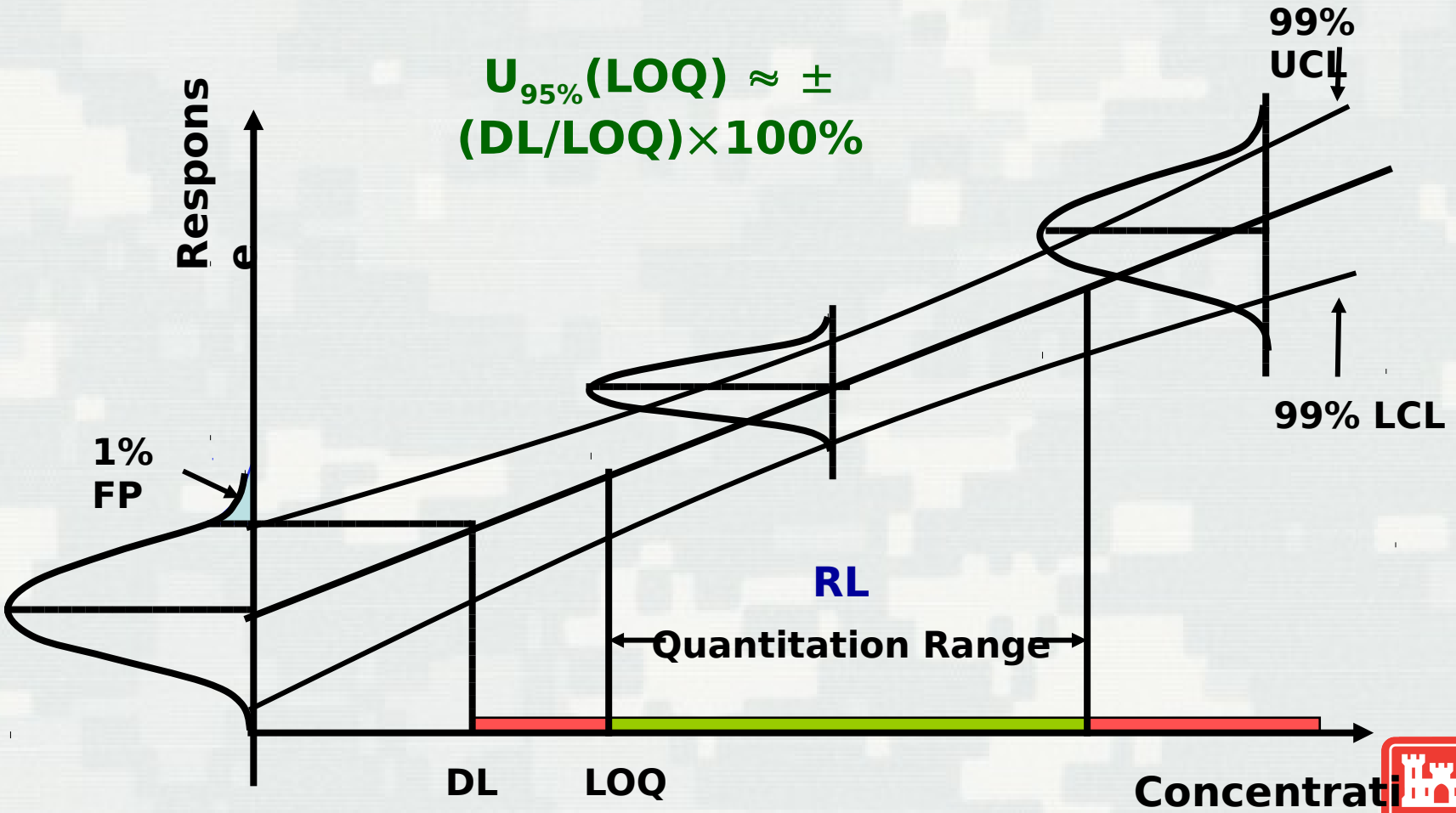
- ***LOQ**: The minimum levels, concentrations, or quantities of a target variable (e.g., target analyte) that can be reported with a specified degree of confidence.*

  – ***NELAC Standard, 5 June 2003***

- ***LOQ (Clarification)**: The lowest concentration that produces a quantitative result within specified limits of precision and bias.*

  – ***DoD QSM V4.1***

Uncertainty vs Concentration



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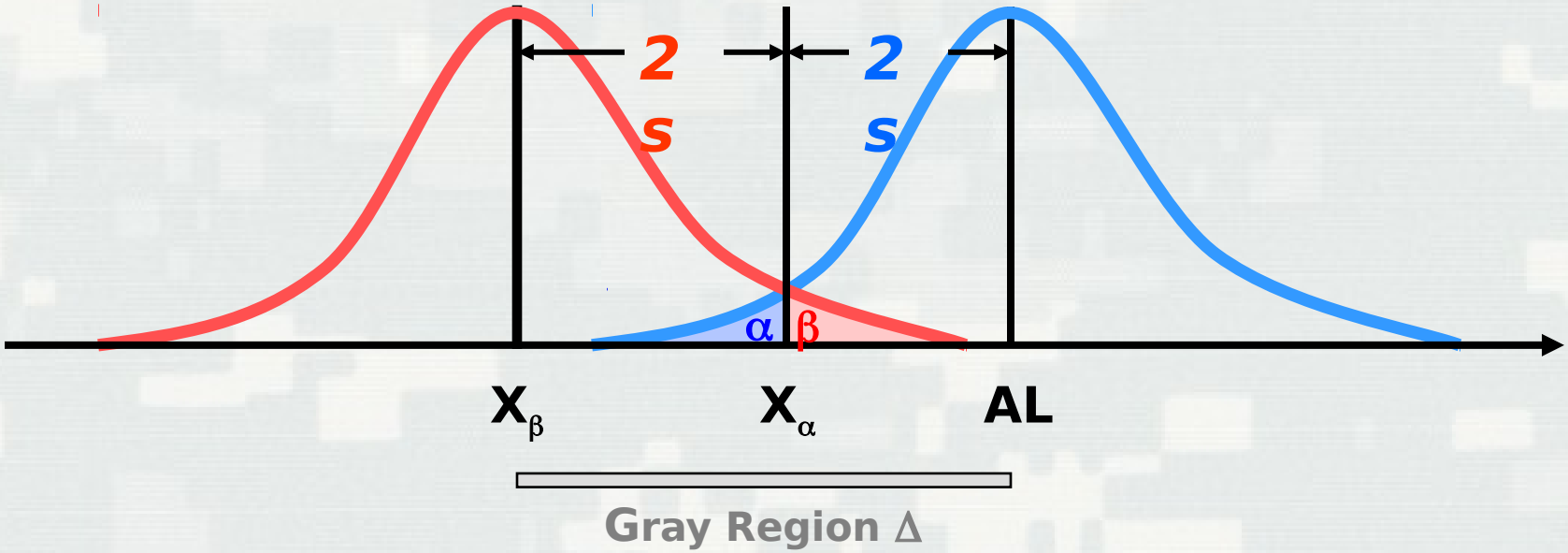
Project MQOs vs Lab MQIs

H_0: X > AL, H_A: X ≤ AL; decision errors $\alpha = \beta = 0.05$



1. *RL ≤ (AL – 4s) × %R and s ≤ (AL – RL / %R) / 4 < 25%.*
2. *LOQ ≤ RL if both have same precision and bias.*

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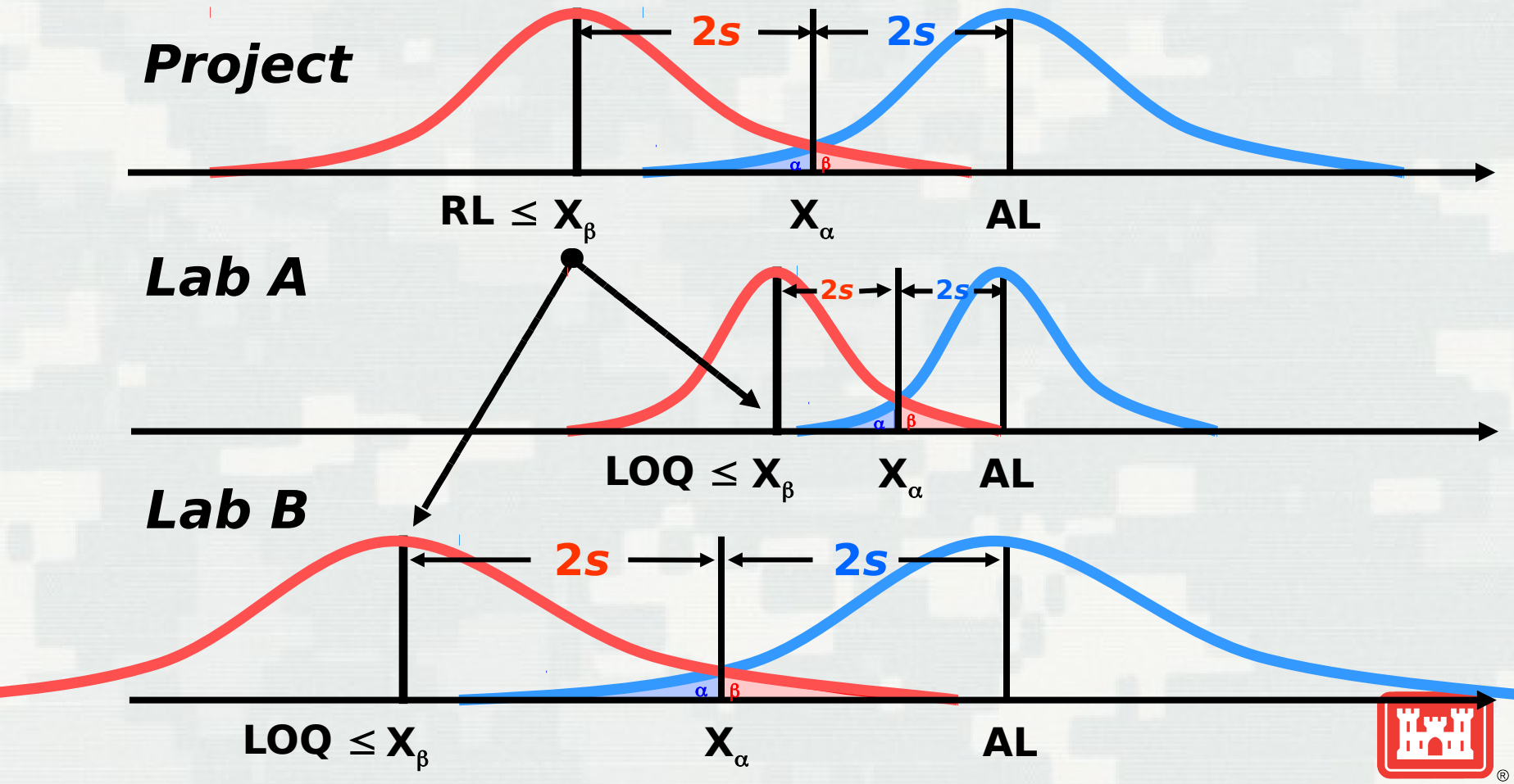
Example for Establishing MQOs

- *What are the MQOs required for reliable ($\alpha = \beta = 0.05$) disposal of IDW to a landfill if AL < 50 ppm?*
  - ***Minimum Project MQOs Needed**:*
    AL: 50 ppm
    Tolerable Decision Errors: $\alpha = \beta = 0.05$
    Precision: LCS CL = $\pm$ 30% $\Rightarrow$ s = 10% = 5 ppm
    Bias: mean LCS %R = 100% from publications
    Reporting Limit: RL = (AL – 4s) × %R = 30 ppm
  - ***Minimum Laboratory MQIs Needed**:*
    LOQ $\leq$ 30 ppm if precision = $\pm$ 30% and %R = 100%
    LOQ $\leq$ 15 ppm if precision = $\pm$ 30% but %R = 50%

Project RL vs Lab LOQ



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Issues

- *Old Rules of Thumb of "LOQ = Lowest Cal. Std. = 3 × MDL ≤ RL ≤ 1/5 ~ 1/10 × AL" may not be adequate.*
- *Laboratory with LOQ ≤ RL does not necessarily meet project MQO for sensitivity. Precision & bias must also be considered.*
- *Scientifically valid and consistent procedures are needed for establishing laboratory performance data for precision, bias, and sensitivity.*
- *Total data quality, including field sampling and laboratory analysis, needs to be considered for reliable project planning and decision making.*
- *Laboratory is not liable for compensation of sampling errors. Better sampling design and techniques (e.g., IMS) are needed to reduce field sampling errors.*

Case Study

- *Groundwater investigation of a potential source of benzo(a)pyrene contamination. Developing MQOs for precision, bias, and sensitivity & screening contract labs.*
  - *AL: MCL = 0.2 ppb; Expected data quality: LCS %R = 81.3% & s = 9.5% from DoD QSM V4.1; Decision errors: $\alpha = \beta = 0.05$*
  - *RL ≤ (AL – 4s) × %R = **0.10** ppb if %R ≥ **81%** & s ≤ **9.5%***
- *DoD ELAP Accredited **Lab X**:*
  - *SW 8270: LOQ = **0.2** ppb; LCS %R = **82.5%** & s = **16.2%***
  - *LOQ ≤ (AL – 4s) × %R = (0.2 – 4 × 16.2% × 0.2) × 82.5% = 0.058 ppb*
- *DoD ELAP Accredited **Lab Y**:*
  - *SW 8270: LOQ = **0.2** ppb; LCS %R = **84.5%** & s = **9.8%***
  - *SW 8310: LOQ = **0.1** ppb; LCS %R = **92.5%** & s = **9.5%***

Summary

- *Simple, reliable, and cost-effective procedure for establishing MQOs based on project-specific action level, expected laboratory data quality, and tolerable decision errors.*
- *MQOs established based on LCS control limits are minimum data quality requirements. More stringent MQOs are needed to cover sample matrix interferences and field sampling errors.*
- *A useful tool for screening contract laboratories prior to contract award.*
- *LOQ ≤ RL may not meet DQOs.*

Overall Review

- *Introduction – Overview*
- *Limit of Detection (LOD)*
- *Limit of Quantitation (LOQ)*
- *Laboratory Control Sample (LCS)*
- *Project Applications*

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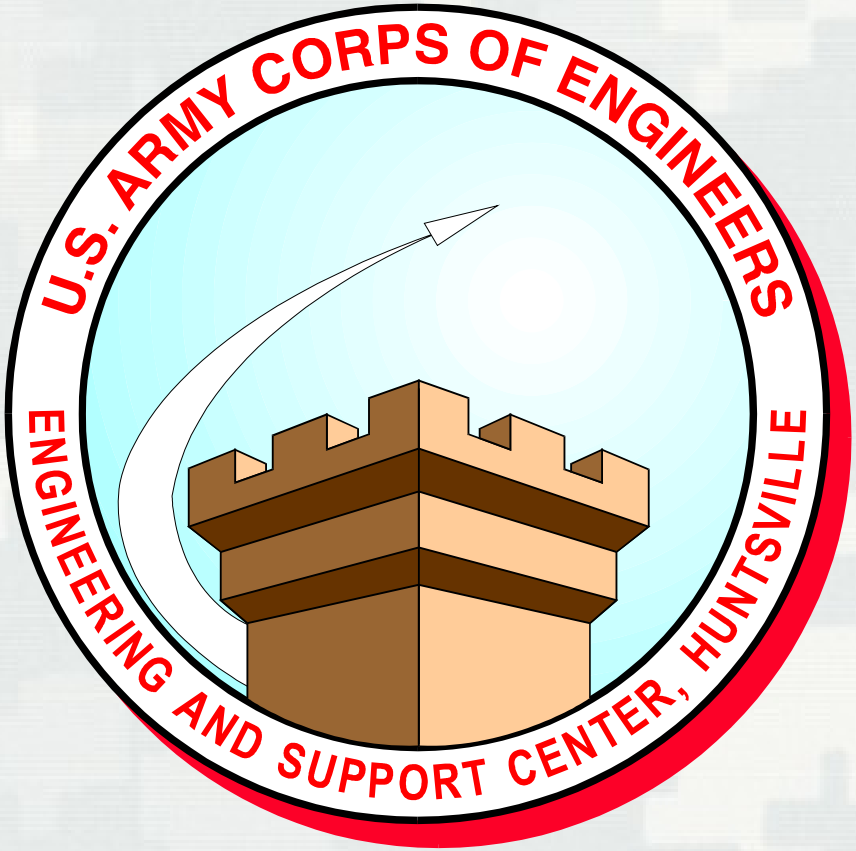
Questions?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